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Artificial intelligence shows comparable or improved performance to traditional risk models in predicting atrial fibrillation after cryptogenic stroke

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Abstract

Background and Aims: Detecting subclinical atrial fibrillation (AF) and initiating anticoagulation therapy are critical for secondary stroke prevention after cryptogenic stroke. This study aimed to evaluate the effectiveness of traditional AF risk scores commonly used in clinical practice and compare with an artificial intelligence (AI)-driven ECG-derived AF prediction score. **Methods:** A retrospective tertiary care center study identified all cryptogenic stroke/TIA patients admitted between 2017-2023 who received an implantable cardiac monitor (ICM). The European Society of Cardiology (ESC)-recommended risk factors and risk score components (i.e.,CHA_2DS_2-VA, Brown ESUS-AF, and HAVOC) from the 2024 guidelines for AF management, were analyzed using multivariate logistic regression to predict AF within one-year post-ICM insertion. The predictive performance of these risk scores and an AI-driven ECG algorithm for AF detection was assessed and compared. **Results:** 230 cryptogenic stroke/TIA patients underwent ICM insertion. Only age (OR: 1.033, 95%CI 1.002-1.066) was associated with an increased likelihood of AF detection within one-year post-ICM insertion. The ECG-AI score demonstrated higher predictive power over CHA_2DS_2-VA and HAVOC (p=.002), and was the only score exceeding an AUROC value of 0.7, but did not outperform Brown ESUS-AF (p=.210). Patients with high scores had a more than two-fold increased likelihood of AF detection (HR: 2.7, 95%CI 1.2-5.8, p=.01). **Conclusions:** In patients with cryptogenic stroke receiving an ICM, the ECG-AI score showed modest discrimination for AF detection, outperforming CHA_2DS_2-VA and HAVOC, but not Brown ESUS-AF. Age was the only significant clinical predictor. These findings indicate a possible role for AI-driven ECG analysis in risk stratification.

Keywords

cryptogenic stroke, atrial fibrillation, ICM, risk score, prediction, implantable cardiac monitor, artificial intelligence, electrocardiogram, digital health

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Introduction

Approximately one-third of ischemic stroke patients have no identifiable cause and are classified as cryptogenic.[1] Detecting atrial fibrillation (AF) as a potential cause is essential to initiate appropriate treatment strategies, such as oral anticoagulation therapy.[2] Prolonged electrocardiographic (ECG) monitoring with implantable cardiac monitors (ICMs) significantly increases AF detection rates compared to standard 24-hour ECG monitoring, identifying AF in up to 30% of cryptogenic stroke patients after three years of monitoring.[3] Both the European Society of Cardiology (ESC) and the American Heart Association (AHA) recommend prolonged cardiac monitoring for this purpose.[2,4]

The latest ESC guidelines for the management of AF emphasize the use of prolonged cardiac monitoring based on risk factors such as increasing age, left atrial enlargement, cortical stroke location, large or small vessel disease, an increased number of premature atrial contractions per 24 h, rhythm irregularities, and risk stratification scores such as CHA_2DS_2-VA, Brown ESUS-AF, HAVOC, and C_2HEST.[2] The use of artificial intelligence (AI) in healthcare has expanded significantly in recent years, demonstrating its potential to enhance diagnostic and predictive capabilities. One notable application is the use of AI in analyzing 12-lead ECGs. Studies have shown that AI algorithms can effectively identify subtle patterns in ECGs recorded during sinus rhythm, enabling the identification of patients at risk for subclinical AF. This approach has the potential to improve risk stratification, particularly in patients who may not yet exhibit clinical AF.[5–7] These risk scores and factors could optimize resource allocation by prioritizing invasive, prolonged cardiac monitoring for high-risk patients. This is particularly relevant given evidence that AF detection is not distributed equally across sociodemographic groups, with lower detection reported in Black and Hispanic patients despite a higher burden of AF risk factors. Targeted monitoring may therefore help reduce under-detection in groups at greater risk of being missed, while also limiting unnecessary monitoring in low-risk patients and allowing clinicians to focus on alternative potential stroke mechanisms.[8,9]

The current study aims to identify clinical risk factors associated with AF diagnosis after cryptogenic stroke or transient ischemic attack (TIA) and evaluate the effectiveness of traditional AF risk scores compared with an AI-driven ECG AF risk score. This will enable more targeted (prolonged) cardiac monitoring and treatment of high-risk patients.

Methods

Study design

A retrospective study was conducted in the single tertiary care center Ziekenhuis Oost-Limburg (Genk, Belgium). Approval from the medical ethics committees of Ziekenhuis Oost-Limburg and Hasselt University (Hasselt, Belgium) were obtained (reference: 20/0037R, 2020/038), with a waiver for informed consent.

Study population

All consecutive cryptogenic stroke or TIA patients admitted to our center between January 1, 2017 and January 1, 2023, who received an ICM were retrospectively identified. Only the index event was taken into consideration in case of stroke or TIA recurrence during this period. All patients underwent a complete evaluation to determine the stroke cause. This diagnostic workup included brain imaging, non-invasive vascular imaging, routine laboratory investigations, transesophageal echocardiography, 12-lead ECG, ECG monitoring for at least 24 hours during hospital stay, and ambulatory 7-day Holter.[10] If there was no determining pathology, the stroke was classified as cryptogenic according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.[11]

Data collection

Demographic and clinical data were collected from the electronic medical records (HiX, Chipsoft, Amsterdam, The Netherlands). The following parameters were assessed: confirmed detection of AF on ICM lasting more than 30 seconds, OAC use, stroke or TIA recurrence, one-year mortality, cumulative number of premature atrial contractions over the entire 7-day Holter monitoring period, and comorbidities (e.g., hypertension, diabetes, …). Furthermore, the following risk scores were calculated. CHA_2DS_2-VA (range: 0-8; 1 point each for congestive heart failure, hypertension, diabetes, vascular disease, and age (65-74); 2 points each for age (≥75 years) and prior stroke/TIA), Brown ESUS-AF (range: 0-4; 1 point for age (65-74); 2 points each for age (≥75 years) and moderate or severe left atrial enlargement), HAVOC (range: 0-14; 1 point each for peripheral vascular disease and obesity (body mass index >30); 2 points each for hypertension, age (≥75 years), valvular heart disease, and coronary artery disease; 4 points for congestive heart failure). Patients missing any variables required to calculate a given risk score were excluded from that analysis. The C_2HEST score, although referenced in ESC

guidelines, was not evaluated because several required components were not collected in this cohort, making retrospective calculation infeasible. Cut-off values for the risk scores were determined in accordance with the ESC recommendations for Brown ESUS-AF and HAVOC and based on findings from previous studies for CHA_2DS_2-VA.[8,12,13] Finally, the ECG-AI algorithm was applied to the first available 10-second 12-lead ECG in sinus rhythm obtained within 30 days of the index stroke or TIA. Raw electrocardiographic data were extracted from the MUSE data management system together with the electrocardiographic parameters provided by the GE Marquette software. All ECGs were acquired at a sampling rate of 500 Hz. The algorithm, trained internally and externally validated as described by Gruwez and Barthels et al., estimates the risk of underlying AF from a 12-lead ECG in sinus rhythm within 31 days. A detailed description of the model development, including training and validation procedures, has been published previously.[7] The primary endpoint was AF detection within one-year post-ICM insertion in cryptogenic stroke or TIA patients. AF detection was assessed over this one-year period, which represented the minimum duration of continuous monitoring available for all patients and ensured uniform follow-up and consistent monitoring duration across the cohort. Labeling of the ICM data was performed in two steps. First, the ICM device algorithm identified episodes of heart rhythm irregularity potentially consistent with AF or other arrhythmias. Subsequently, these episodes were adjudicated by dedicated healthcare professionals from the remote monitoring team according to standard clinical practice, blinded to the ECG-AI score.

Statistical analysis

The acquired data was analyzed using Statistical Package for Social Sciences release 29.0 (IBM® SPSS® Inc., Chicago, Illinois, USA) and RStudio version 2023.12.1 +402 (Posit, Boston, Massachusetts, USA). All assumptions were checked before carrying out the concerning statistical test. A p-value$<$ .05 was considered statistically significant. The Shapiro-Wilk statistic evaluated the normality of the continuous data.

Continuous data were expressed as means ± standard deviation or medians and interquartile range (IQR) when appropriate and were compared with an unpaired t-test or Mann-Whitney U test. Categorical data were expressed as absolute numbers and percentages and compared with the Pearson Chi-square or Fisher's exact test when appropriate.

Furthermore, univariate logistic regression analysis was conducted for each comorbidity separately, with AF within one-year post-ICM insertion as the outcome. Subsequently, an exploratory multivariate logistic regression analysis was performed, incorporating significant covariates ($p < .25$) and applying backward elimination until only significant variables remained ($p < .05$). Finally, the risk scores were evaluated in our population using the area under the receiver operating characteristics curve (AUROC), sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). The discrimination of each risk score for AF was assessed using Harrell's concordance index (C-index) (higher values indicating better concordance).[14] DeLong's test was used to perform pairwise comparisons of AUROCs, including only patients with both scores available for each comparison. As an exploratory analysis in this study, the optimal cut-off value of the ECG-AI risk score was derived using the Youden index to classify patients as low or high risk for underlying subclinical AF. The time to first AF detection following ICM insertion was analyzed using Cox regression to compare low- and high-risk groups, as defined by the ECG-AI score and its training population-based and optimal cut-off value. The results were visualized using a Kaplan-Meier curve.

Results

Demographics

Among 924 cryptogenic stroke or TIA patients admitted during the study period, 230 received an ICM and were included in the analyses. Mean follow-up time was 934 ± 338 days post-ICM insertion. Most (199 (86.5%)) patients received a Reveal LINQ (Medtronic, Minneapolis, MN, USA), of which 15 patients received the Reveal LINQ II. Furthermore, 25 (10.9%) patients had a BIOMONITOR (Biotronik, Berlin, Germany) inserted, and 6 (2.6%) a Confirm Rx (Abbott, Lake County, IL, USA). AF was detected in 40 (17.4%) patients within one year after ICM insertion after a median of 65 [19 - 227] days post-ICM insertion. Table 1 shows the between-group differences in baseline characteristics.

Patients with AF detected within one-year post-ICM insertion were older ($p = .01$), had a higher score on the NIH Stroke Scale on admission ($p = .02$), a higher Brown ESUS-AF score ($p = .004$), a higher ECG-AI score ($p < .001$), and had more premature atrial contractions on AF-negative 7-day Holter ($p = .002$). Smoking and hypercholesterolemia were less prevalent in those with AF detected ($p = .009$ and $p = .045$, respectively). Notably, 13 (5.7%) patients were reported with a stroke or TIA recurrence after ICM insertion with no difference ($p = .475$) between those with and without AF detected.

Table 1. Baseline characteristics of study population.

Characteristic	All (n = 230)	No AF[a] (n = 190)	AF (n = 40)	*p*-value[b]
Age, years	67 [57 - 76]	66 [57 - 74]	74 [66 - 79]	.010
Sex, female	97 (42.2%)	82 (43.2%)	15 (37.5%)	.510
Index event				.664
Stroke	178 (77.4%)	146 (76.8%)	32 (80.0%)	
TIA	52 (22.6%)	44 (23.2%)	8 (20.0%)	
Prior stroke or TIA	34 (14.8%)	29 (15.3%)	5 (12.5%)	.655
Recurrent stroke or TIA[c]	13 (5.7%)	12 (6.3%)	1 (2.5%)	.475
Score on NIH Stroke Scale	2 [0 - 4]	1 [0 - 4]	3 [1 - 6]	.020
ASPECT	10 [10 - 10]	10 [10 - 10]	10 [9 - 10]	.101
One-year mortality	3 (1.3%)	1 (0.5%)	2 (5.0%)	.079
Days between stroke - death	885 ± 463	983 ± 389	623 ± 632	.497
Days between stroke – ICM insertion	103 [69 - 156]	102 [70 - 156]	110 [60 - 154]	.552
Comorbidities				
Current smoker	54 (23.5%)	51 (26.8%)	3 (7.5%)	.009
Excessive alcohol consumption[d]	18 (7.8%)	14 (7.4%)	4 (10.0%)	.527
Hypertension	142 (61.7%)	118 (62.1%)	24 (60.0%)	.803
Diabetes mellitus	37 (16.1%)	34 (17.9%)	3 (7.5%)	.104
Hypercholesterolemia	136 (59.1%)	118 (62.1%)	18 (45.0%)	.045
Obesity[e]	56 (24.3%)	44 (23.2%)	12 (30.0%)	.359
Congestive heart failure	11 (4.8%)	10 (5.3%)	1 (2.5%)	.694
Chronic kidney disease	30 (13.0%)	26 (13.7%)	4 (10.0%)	.529
Peripheral vascular disease	22 (9.6%)	20 (10.5%)	2 (5.0%)	.383
Prior myocardial infarction	14 (6.1%)	11 (5.8%)	3 (7.5%)	.715
Atherosclerotic disease	129 (56.1%)	104 (54.7%)	25 (62.5%)	.369
PFO	68 (30.8%)	58 (31.5%)	10 (27.0%)	.589
Closed PFO (n = 68)	17 (25.0%)	15 (25.9%)	2 (20.0%)	1.000
Valvular heart disease	38 (16.5%)	31 (16.3%)	7 (17.5%)	.855
Coronary artery disease	47 (20.4%)	39 (20.5%)	8 (20.0%)	.940
Premature atrial contractions (7-day Holter)	386 [134 - 1839]	316 [118 - 1220]	1815 [471 - 4264]	.002
LVEF:				.476
Normal	220 (95.7%)	180 (94.7%)	40 (100.0%)	
Low-normal	9 (3.9%)	9 (4.7%)	-	
Reduced	1 (0.4%)	1 (0.5%)	-	
Left atrium size:				.316
Normal	181 (83.4%)	150 (84.7%)	31 (77.5%)	
Mild	28 (12.9%)	22 (12.4%)	6 (15.0%)	
Moderate dilated	8 (3.7%)	5 (2.8%)	3 (7.5%)	
Risk scores				
CHA_2DS_2-VA	4 [3 - 5]	4 [3 - 5]	5 [4 - 5]	.231
Brown ESUS-AF	1 [0 - 2]	1 [0 - 1.5]	1 [1 - 2]	.004
HAVOC	2.5 [1.75 - 4]	2 [1 - 4]	3 [2 - 4]	.253
ECG-AI	5.6 [1.9 - 13.9]	4.9 [1.7 - 11.8]	14.0 [5.4 - 26.1]	<.001

Data are expressed as mean ± SD, number (percentage), or median (IQR).
[a]AF detected within one-year post-ICM insertion.
[b]Pearson Chi-Square test, Fisher's exact test, and Mann-Whitney U test were used in the analyses.
[c]Recurrent stroke or TIA after ICM insertion.
[d]More than two units/day.
[e]BMI ≥ 30.
AF, atrial fibrillation; ASPECT, Alberta stroke program early CT score; ICM, implantable cardiac monitor; LVEF, left ventricular ejection fraction; NIH Stroke scale, national institutes of health stroke scale; PFO, patent foramen ovale; TIA, transient ischemic attack.

Predictors of atrial fibrillation

An exploratory multivariate logistic regression analysis with backward elimination was conducted to evaluate the impact of ESC-recommended risk factors and components of the risk scores on the likelihood of detecting AF within one-year post-ICM insertion. Age (OR: 1.033, 95%CI: 1.002 – 1.066) was the only factor associated with an increased likelihood of AF detection (Table 2).

Table 2. Predictors of atrial fibrillation within one year after ICM insertion.

Predictor	Univariate OR (95% CI)	*p*-value
Age	1.033 (1.002 - 1.066)	.040
Diabetes	0.372 (0.108 - 1.277)	.116
Left atrial enlargement[a]	1.613 (0.691 - 3.765)	.269
Peripheral vascular disease	0.447 (0.100 - 1.996)	.292
Obesity	1.422 (0.668 - 3.027)	.361
Congestive heart failure	0.462 (0.057 - 3.711)	.467
Prior stroke or TIA	0.793 (0.287 - 2.193)	.655
Hypertension	0.915 (0.456 - 1.838)	.803
Valvular heart disease	1.088 (0.442 - 2.681)	.855
Premature atrial contractions during 7-day Holter	1.000 (1.000 - 1.000)	.914
Coronary artery disease	0.968 (0.413 - 2.267)	.940

[a]Moderate or severe.

Performance of the risk scores

The ability of the risk scores (i.e., CHA_2DS_2-VA, Brown ESUS-AF, and HAVOC) to predict AF within one year following a cryptogenic stroke or TIA was limited, as reflected by low AUROC and C-index values in Table 3 and visualized in ROC curves in Figure 1. None of the risk scores demonstrated acceptable performance, with no AUROC exceeding 0.7. The only risk score exceeding this threshold was the ECG-AI score, with an AUROC of .710. Moreover, it had the highest NPV and C-index. Pairwise comparisons using DeLong's test indicated that the ECG-AI score had a significantly higher AUROC than the CHA_2DS_2-VA ($p = .002$) and HAVOC ($p = .002$) scores, but not compared with the Brown ESUS-AF score ($p = .210$). The Brown ESUS-AF score also showed a significantly higher AUROC than CHA_2DS_2-VA ($p = .030$). The remaining pairwise comparisons did not reach statistical significance.

While the AUROC of the ECG-AI score tended to be slightly higher for longer AF episode durations (AUROC: AF > 6 min = .712 [95%CI .569 - .856], AF > 1h = .747 [95%CI .588 - .907], AF > 6h = .714 [95%CI .463 - .964]), DeLong's test indicated that these differences were not statistically significant (all $p > .05$).

As an exploratory analysis, the optimal cut-off value for the ECG-AI score was determined to be 13.4% (Youden index = .359), yielding a sensitivity of 54.8% (95%CI 36.0% - 72.7%), specificity of 80.0% (95%CI 72.4% - 86.3%), PPV of 37.8% (95%CI 23.8% - 53.5%), and NPV of 88.9% (95%CI 82.1% - 93.8%). This threshold is higher than the optimal cut-off identified in the training population (i.e., 5.6%, Youden index = .261). Patients with a high ECG-AI risk score (based on the training-population threshold ≥5.6%) had a more than two-fold increased risk of subsequent AF detection within one year after ICM insertion (HR: 2.7, 95%CI 1.2 - 5.8, p=.01, Figure 2). The score was low in 49.7% and high in 50.3% of patients, with AF detected in 10.6% and 25.6%, respectively. Patients with a high ECG-AI risk score (based on the optimal threshold in this selected ICM population ≥ 13.4%) had a four-fold increased risk of subsequent AF detection within one year after ICM insertion (HR: 4.0, 95%CI 2.0 - 8.1, $p < .001$). The score was low in 73.7% and high in 26.3% of patients, with AF detected in 11.1% and 37.8%, respectively.

Table 3. Diagnostic performance of risk scores for the prediction of atrial fibrillation within one year after ICM insertion.

	CHA_2DS_2-VA ≥ 4 (n = 230)	Brown ESUS-AF ≥ 2 (n = 217)	HAVOC ≥ 4 (n = 230)	ECG-AI ≥ 5.6 (n = 171)
AUROC	.559 (.465 - .653)	.639 (.543 - .734)	.557 (.469 - .645)	.710 (.608 - .811)
Sensitivity	77.5 (61.5 - 89.2)	45.0 (29.3 - 61.5)	47.5 (31.5 - 63.9)	71.0 (52.0 - 85.8)
Specificity	34.7 (28.0 - 42.0)	75.1 (68.1 - 81.3)	62.1 (54.8 - 69.0)	54.3 (45.7 - 62.7)
PPV	20.0 (14.0 - 27.2)	29.0 (18.2 - 41.9)	20.9 (13.1 - 30.7)	25.6 (16.8 - 36.1)
NPV	88.0 (78.4 - 94.4)	85.8 (79.3 - 90.9)	84.9 (77.8 - 90.4)	89.4 (80.8 - 95.0)
C-index	.560 (.478 - .643)	.630 (.551 - .709)	.557 (.480 - .633)	.683 (.596 - .770)

Values are presented with 95% confidence intervals in parentheses. AUROC, area under receiver operating characteristic curve; C-index, Harrell's concordance index; ICM, implantable cardiac monitor; NPV, negative predictive value; PPV, positive predictive value.

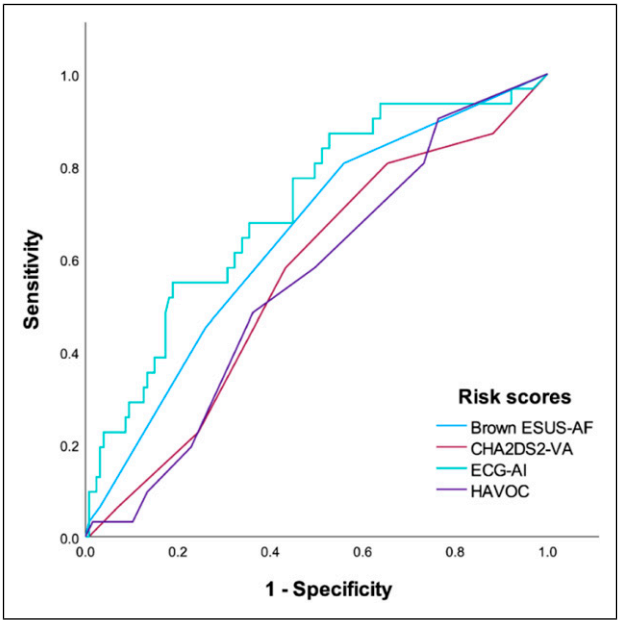

Figure 1. ROC curve of risk scores to predict atrial fibrillation during follow-up of cryptogenic stroke and TIA patients with an ICM. The Brown ESUS-AF, CHA_2DS_2-VA, HAVOC scores, and ECG-AI score to predict AF within one-year post-ICM insertion.

Discussion

This study aimed to identify clinical risk factors associated with AF diagnosed using ICM after cryptogenic stroke or TIA. Additionally, it evaluated the effectiveness of current clinical risk scores compared to an AI-driven ECG generated risk score to predict AF in clinical practice.

AF was detected in 17.4% of cryptogenic stroke or TIA patients within one year following ICM insertion. This rate exceeds the ones reported in the CRYSTAL-AF and STROKE-AF study (i.e., 12.4% and 12.1%), but aligns with findings

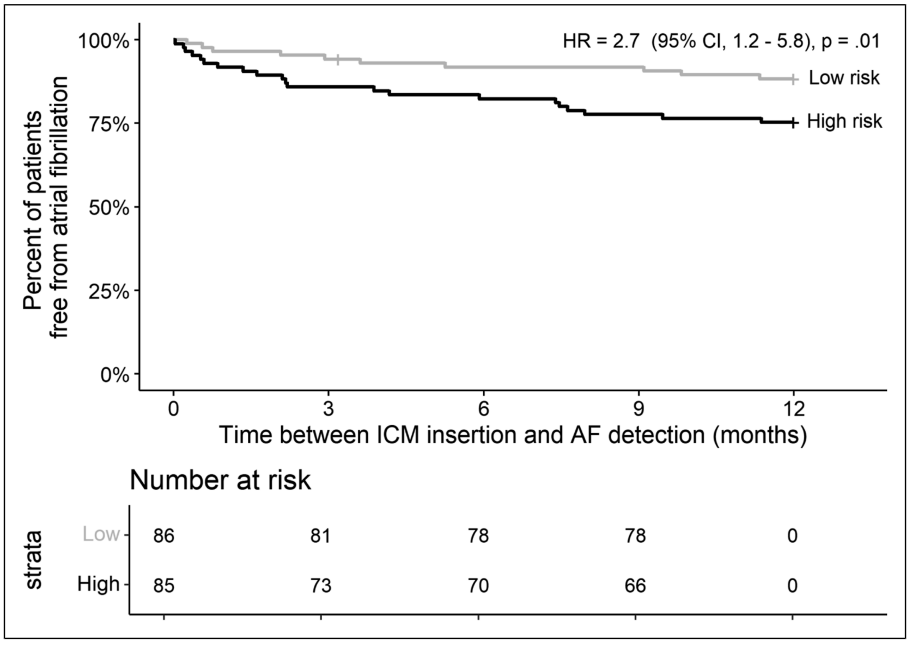

Figure 2. Time to first detection of AF after ICM insertion. High risk patients (ECG-AI score $\geq$ 5.6%) have a 2.7-fold increased risk of AF detection within one year post-ICM insertion compared to low risk patients (ECG-AI score $<$ 5.6%).

from more recent studies, corroborating the need for prolonged cardiac monitoring.[3,13,15,16] Patients with AF were older and exhibited a higher prevalence of premature atrial contractions, as well as increased NIHSS and Brown ESUS-AF scores. Stroke or TIA recurrence rate after ICM was 5.7%. These recurrence rates were in line with those reported in literature.[17,18] Older age was associated with a higher likelihood of AF detection, highlighting its role as a significant risk factor in our multivariate analysis. However, given the limited number of AF events, these findings should be considered exploratory. Although age is included in all ESC-recommended risk scores, these established scores demonstrated suboptimal performance for AF prediction in our cohort.

Despite significantly higher Brown ESUS-AF scores in patients with AF detected within one-year post-ICM insertion, none of the clinically recommended scores (including CHA_2DS_2-VA and HAVOC) demonstrated acceptable discriminatory power for AF prediction, as all AUROC values fell below the generally accepted threshold of 0.7. This likely reflects that CHA_2DS_2-VA and HAVOC capture general comorbidity burden rather than atrial-specific substrate, whereas the Brown ESUS-AF score incorporates a more directly relevant marker of atrial cardiomyopathy, namely severe left atrial enlargement, which may explain its comparatively better performance. Nevertheless, their low discriminatory power aligns with previous literature and highlights the ongoing challenge of identifying individuals at risk of subclinical AF using conventional clinical risk scores.[8,13]

In contrast, the ECG-AI score exhibited stronger predictive performance, with an AUROC just above 0.7, and high-risk patients showing more than a two-fold increased likelihood of AF detection within one year after ICM insertion compared to low-risk patients. An ECG-AI score of 5.6 resulted in an NPV of 89.4% allowing good discrimination of patients with a very low likelihood of AF. In this study, 85 (49.7%) patients had an ECG-AI score < 5.6. During follow-up, AF was detected on ICM in 9 (10.6%) patients. With the exception of one patient, all AF episodes lasted one hour or less; a single patient had an episode exceeding six hours in duration. The ECG-AI score could therefore be applied to select patients in whom AF is unlikely or clinically insignificant, thereby sparing them from the need for costly ICMs.

The ECG-AI score threshold of 5.6% was originally derived from the training population in which AF detection relied on 12-lead ECG findings. Importantly, the training and testing cohorts differed not only in population but also in outcome ascertainment. The training cohort consisted of all patients presenting to the hospital for any indication with a normal baseline ECG, in whom the presence or absence of AF was determined based on AF occurrence on a subsequent in-hospital 12-lead ECG recording. In contrast, the testing cohort in this study comprised high-risk patients with cryptogenic stroke or TIA who underwent long-term rhythm monitoring using ICMs, providing a more sensitive and clinically robust method for AF detection over extended follow-up.

In our exploratory analysis, we aimed to determine the optimal threshold for our high-risk subgroup with prolonged rhythm monitoring. The threshold increased to 13.4%, resulting in increased specificity and PPV. Furthermore, patients with a high score ($\geq$13.4%) now had a four-fold increased risk of AF identified within one year post-ICM insertion compared to those with a low score.

These differences in population and reference standard for AF detection likely explain the observed variation in optimal thresholds for the ECG-AI score. This highlights the need for recalibration when applying the model across settings with different populations and outcome definitions, and underscores the importance of external validation in cohorts with standardized, continuous AF monitoring to ensure robust and generalizable performance prior to clinical implementation.

This study highlights the potential of AI-driven models to enhance risk stratification of patients for identifying AF post cryptogenic stroke. While derived from a selected cohort undergoing ICM implantation, these findings support further evaluation of such approaches with the long-term goal of optimizing the allocation of invasive cardiac monitoring methods in post-stroke patients.

An AI-driven approach could offer a novel, scalable strategy for identifying high-risk individuals who may benefit from intensive monitoring. This approach also identifies a group of low-risk patients who do not need continuous invasive monitoring but can easily and safely be monitored using regular spot-check measurements with ambulatory ECG or PPG technology. This approach could improve resource allocation to high-risk patients, reduce unnecessary expensive and invasive monitoring in the low-risk population which can be safely replaced by low cost spot-check measurements and reducing burden on remote monitoring staff. However, further research is needed on how to integrate the ECG-AI score into routine clinical practice and determine prospectively its impact on cost/benefit and patient outcomes.[6,19–21] Implementation will require appropriate infrastructure, including high-quality digital ECG systems utilizing a sampling frequency of 500 Hz, secure data storage, and computational resources, as well as workflow integration. External validation in diverse populations and healthcare settings will be essential to ensure generalizability, and prospective studies should assess not only predictive performance but also effects on clinical decision-making. Importantly, improved AF detection does not necessarily translate into improved clinical outcomes, as the net benefit of anticoagulation in device-detected AF remains dependent on absolute stroke risk and bleeding trade-offs.[22]

Finally, incorporating non-ECG–derived parameters may further enhance model performance, as AF is not solely an electrical disorder characterized by electrophysiological abnormalities but also a clinical manifestation of cardiomyopathy, reflecting broader functional and structural remodeling, including atrial fibrosis and dilation.[23–25]

Our study has several limitations that should be considered when interpreting the results. First, the predictive performance of the established clinical risk scores in our study differed from prior research, likely due to variations in patient characteristics, AF burden, and methodology. The CHA_2DS_2-VA score, originally designed to assess stroke risk in AF patients, was not intended to predict AF occurrence and showed reduced sensitivity in our ICM cohort.[26] The HAVOC and Brown ESUS-AF scores were developed in populations with lower AF detection rates, where long-term ICM monitoring was not standard.[27,28] Additionally, other studies included younger, healthier cohorts with different comorbidity profiles when evaluating these risk scores.[8,13,18] These differences highlight the limited generalizability of existing scores to cryptogenic stroke patients with high comorbidity burdens, emphasizing the need for tailored predictive models. Second, the retrospective design may introduce indication bias, as the decision to insert ICMs was based on clinical judgment. ICMs were more commonly inserted in younger patients, males, those who experienced a stroke (as opposed to a TIA), and patients with a PFO. This indicates that ECG-AI performance was assessed within a selected patient population, which could hinder generalizability. Moreover, this may have influenced the performance of age-weighted clinical risk scores (i.e., CHA_2DS_2-VA, Brown ESUS-AF, and HAVOC) relative to ECG-AI, as these scores may perform differently in an older, unselected post-stroke population. Furthermore, the median time to ICM implantation was 103 days post-stroke, which may have led to missed AF episodes during this interval. Additionally, given the retrospective nature of the study, not all variables recommended by the latest ESC guidelines or the components of the suggested risk scores were available in our dataset, potentially limiting our ability to comprehensively assess and stratify patients' risk. Furthermore, an ECG-AI score could not be derived for 59 patients, who were therefore excluded from the ECG-AI-based analyses. This was due to the absence of an ECG within 30 days after the stroke or TIA event (31 patients) or an ECG of insufficient quality (i.e., due to low sampling rate) (28 patients). Finally, the study was conducted at a single tertiary care center, which could reduce the generalizability of our findings.

Conclusion

This retrospective study demonstrated that an AI-driven algorithm applied to a sinus rhythm ECG had higher but still modest discriminative power than established clinical risk scores such as CHA_2DS_2-VA and HAVOC, though not compared with Brown ESUS-AF. It was able to identify patients with AF identified within one year after ICM insertion following a cryptogenic stroke. Specifically, patients with a high ECG-AI score exhibited a more than two-fold increased likelihood of AF detection compared to low-risk patients. These findings highlight the potential of AI-driven ECG analysis as a risk stratification tool and determine different rhythm monitoring strategies for AF detection in low- and high-risk patient cohorts post-cryptogenic stroke, though further validation in unselected stroke/TIA populations is warranted.

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Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Ziekenhuis Oost-Limburg and Hasselt University (no. 20/0037R, 2020/038), with the need for written informed consent waived.

Author contributions

Conceptualization: all authors; Formal analysis: Femke Wouters, Myrte Barthels; Investigation: Femke Wouters; Methodology: Pieter Vandervoort, Julie Vranken, Femke Wouters; Software: Myrte Barthels; Writing – original draft: Femke Wouters; Writing – review & editing: all authors.

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Data Availability Statement

The protocol and data that support the findings of this study are available from the corresponding author, upon reasonable request. Prof. Dr. Pieter Vandervoort is the guarantor of this work.

References

1. Li LD, Yiin GSD, Geraghty OCD, et al. Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: a population-based study. *The Lancet Neurology* 2015; 14(9): 903–913. https://doi.org/10.1016/S1474-4422(15)00132-5
2. Van Gelder IC, Rienstra M, Bunting KV, et al. ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2024; 2024: 1–101.
3. Sanna T, Diener H-C, Passman RS, et al. Cryptogenic Stroke and Underlying Atrial Fibrillation. *The New England Journal of Medicine* 2014; 370(26): 2478–2486. https://doi.org/10.1056/nejmoa1313600
4. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024; 149(1): e1–e156. https://doi.org/10.1161/cir.0000000000001193
5. Siontis KC, Noseworthy PA, Attia ZI, et al. Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. *Nat Rev Cardiol* 2021; 18(7): 465–478. https://doi.org/10.1038/s41569-020-00503-2
6. Attia ZI, Noseworthy PA, Lopez-Jimenez F, et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. *The Lancet (British edition)* 2019; 394(10201): 861–867. https://doi.org/10.1016/S0140-6736(19)31721-0
7. Gruwez H, Barthels M, Haemers P, et al. Detecting Paroxysmal Atrial Fibrillation From an Electrocardiogram in Sinus Rhythm: External Validation of the AI Approach. *JACC: Clinical Electrophysiology* 2023; 9(8, Part 3): 1771–1782. https://doi.org/10.1016/j.jacep.2023.04.008
8. Ratajczak-Tretel B, Lambert AT, Al-Ani R, et al. Prediction of underlying atrial fibrillation in patients with a cryptogenic stroke: results from the NOR-FIB Study. *J Neurol* 2023; 270(8): 4049–4059. https://doi.org/10.1007/s00415-023-11680-8
9. Laslett DB, Haddad A, Mangrolia H, et al. Racial differences in the incidence of atrial fibrillation after cryptogenic stroke. *Heart Rhythm* 2021; 18(6): 847–852. https://doi.org/10.1016/j.hrthm.2021.01.027
10. McMahon NE, Bangee M, Benedetto V, et al. Etiologic Workup in Cases of Cryptogenic Stroke: A Systematic Review of International Clinical Practice Guidelines. *Stroke (1970)* 2020; 51(5): 1419–1427. https://doi.org/10.1161/STROKEAHA.119.027123
11. Adams JHP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993; 24(1): 35–41. https://doi.org/10.1161/01.str.24.1.35
12. Dilaveris PE, Antoniou CK, Caiani EG, et al. ESC Working Group on e-Cardiology Position Paper: accuracy and reliability of electrocardiogram monitoring in the detection of atrial fibrillation in cryptogenic stroke patients: In collaboration with the Council on Stroke, the European Heart Rhythm Association, and the Digital Health Committee. *European Heart Journal - Digital Health* 2022; 3(3): 341–358. https://doi.org/10.1093/ehjdh/ztac026
13. Grygorowicz C, Benali K, Serzian G, et al. Value of HAVOC and Brown ESUS-AF scores for atrial fibrillation on implantable cardiac monitors after embolic stroke of undetermined source. *Journal of Stroke and Cerebrovascular Diseases* 2024; 33(1): 107451. https://doi.org/10.1016/j.jstrokecerebrovasdis.2023.107451

14. Harrell FE Jr, Califf RM, Pryor DB, et al. Evaluating the Yield of Medical Tests. *JAMA* 1982; 247(18): 2543–2546.
15. Lu Y, Diao SS, Huang SJ, et al. Insertable cardiac monitors for detection of atrial fibrillation after cryptogenic stroke: a meta-analysis. *Neurol Sci* 2021; 42(10): 4139–4148. https://doi.org/10.1007/s10072-021-05104-6
16. Bernstein RA, Kamel H, Granger CB, et al. Effect of Long-term Continuous Cardiac Monitoring vs Usual Care on Detection of Atrial Fibrillation in Patients With Stroke Attributed to Large- or Small-Vessel Disease: The STROKE-AF Randomized Clinical Trial. *Jama* 2021; 325(21): 2169–2177. https://doi.org/10.1001/jama.2021.6470
17. Hart RG, Catanese L, Perera KS, et al. Embolic Stroke of Undetermined Source: A Systematic Review and Clinical Update. *Stroke* 2017; 48(4): 867–872. https://doi.org/10.1161/STROKEAHA.116.016414
18. Palaiodimou L, Theodorou A, Triantafyllou S, et al. Performance of Different Risk Scores for the Detection of Atrial Fibrillation Among Patients With Cryptogenic Stroke. *Stroke* 2024; 55(2): 454–462. https://doi.org/10.1161/STROKEAHA.123.044961
19. Pipilas D, Friedman SF and Khurshid S. The Use of Artificial Intelligence to Predict the Development of Atrial Fibrillation. *Current cardiology reports* 2023; 25(5): 381–389. https://doi.org/10.1007/s11886-023-01859-w
20. Hygrell T, Viberg F, Dahlberg E, et al. An artificial intelligence-based model for prediction of atrial fibrillation from single-lead sinus rhythm electrocardiograms facilitating screening. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology* 2023; 25(4): 1332–1338. https://doi.org/10.1093/europace/euad036
21. Choi J, Kim JY, Cho MS, et al. Artificial intelligence predicts undiagnosed atrial fibrillation in patients with embolic stroke of undetermined source using sinus rhythm electrocardiograms. *Heart Rhythm* 2024; 21(9): 1647–1655. https://doi.org/10.1016/j.hrthm.2024.03.029
22. McIntyre WF, Benz AP, Becher N, et al. Direct Oral Anticoagulants for Stroke Prevention in Patients With Device-Detected Atrial Fibrillation: A Study-Level Meta-Analysis of the NOAH-AFNET 6 and ARTESiA Trials. *Circulation* 2024; 149(13): 981–988. https://doi.org/10.1161/CIRCULATIONAHA.123.067512
23. Yamaguchi T. Atrial structural remodeling and atrial fibrillation substrate: A histopathological perspective. *Journal of Cardiology* 2025; 85(2): 47–55. https://doi.org/10.1016/j.jjcc.2024.05.007
24. Iwasaki Y-K, Nishida K, Kato T, et al. Atrial Fibrillation Pathophysiology. *Circulation* 2011; 124(20): 2264–2274. https://doi.org/10.1161/circulationaha.111.019893
25. Arabia G, Bellicini MG, Cersosimo A, et al. Ion channel dysfunction and fibrosis in atrial fibrillation: Two sides of the same coin. *Pacing and Clinical Electrophysiology* 2024; 47(3): 417–428. https://doi.org/10.1111/pace.14944
26. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137(2): 263–272. https://doi.org/10.1378/chest.09-1584
27. Kwong C, Ling AY, Crawford MH, et al. A Clinical Score for Predicting Atrial Fibrillation in Patients with Cryptogenic Stroke or Transient Ischemic Attack. *Cardiology* 2017; 138(3): 133–140. https://doi.org/10.1159/000476030
28. Ricci B, Chang AD, Hemendinger M, et al. A Simple Score That Predicts Paroxysmal Atrial Fibrillation on Outpatient Cardiac Monitoring after Embolic Stroke of Unknown Source. *Journal of Stroke and Cerebrovascular Diseases* 2018; 27(6): 1692–1696. https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.01.028

Appendix

Abbreviations

AF	atrial fibrillation
AHA	American Heart Association
AI	artificial intelligence
AUROC	area under the receiver operating characteristics curve
C-index	Harrell's concordance index
ECG	electrocardiogram
ESC	European Society of Cardiology
ICM	implantable cardiac monitor
NPV	negative predictive value
OAC	oral anticoagulation
PFO	patent foramen ovale
PPV	positive predictive value
TIA	transient ischemic attack
TOAST	Trial of Org 10172 in Acute Stroke Treatment.