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CLINICAL RESEARCH

Insertable cardiac monitoring results in higher rates of atrial fibrillation diagnosis and oral anticoagulation prescription after ischaemic stroke

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Aims After an ischaemic stroke, atrial fibrillation (AF) detection allows for improved secondary prevention strategies. This study aimed to compare AF detection and oral anticoagulant (OAC) initiation in patients with an insertable cardiac monitor (ICM) vs. external cardiac monitor (ECM) after ischaemic stroke.

Methods and results Medicare Fee-for-Service (FFS) insurance claims and Abbott Labs device registration data were used to identify patients hospitalized with an ischaemic stroke in 2017–2019 who received an ICM or ECM within 3 months. Patients with continuous Medicare FFS insurance and prescription drug enrolment in the prior year were included. Patients with prior AF, atrial flutter, cardiac devices, or OAC were excluded. Insertable cardiac monitor and ECM patients were propensity score matched 1:4 on demographics, comorbidities, and stroke hospitalization characteristics. The outcomes of interest were AF detection and OAC initiation evaluated with Kaplan–Meier and Cox proportional hazard regression analyses. A total of 5702 Medicare beneficiaries (ICM, $n = 444$; ECM, $n = 5258$) met inclusion criteria. The matched cohort consisted of 2210 Medicare beneficiaries (ICM, $n = 442$; ECM, $n = 1768$) with 53% female, mean age 75 years, and mean CHA_2DS_2-VASc score 4.6 (1.6). Insertable cardiac monitor use was associated with a higher probability of AF detection [(hazard ratio (HR) 2.88, 95% confidence interval (CI) (2.31, 3.59)] and OAC initiation [HR 2.91, CI (2.28, 3.72)] compared to patients monitored only with ECM.

Conclusion Patients with an ischaemic stroke monitored with an ICM were almost three times more likely to be diagnosed with AF and to be prescribed OAC compared to patients who received ECM only.

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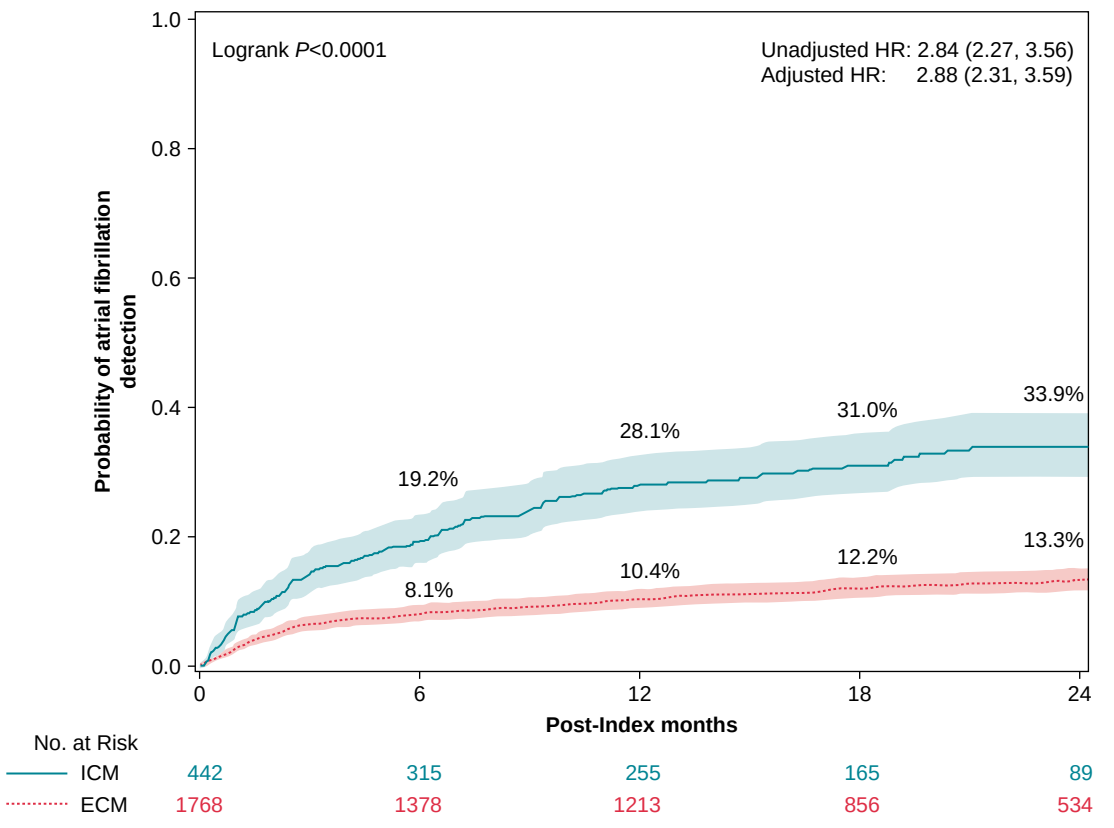
Graphical Abstract



Structured Graphical Abstract graphic element shows 2-year atrial fibrillation incident rates by cardiac monitor method, ICM (solid line) and ECM (dashed line). Rates were estimated using the Kaplan–Meier method. Hazard ratios and 95% CIs estimated by Cox proportional hazard models are also shown.

Keywords Stroke • Atrial fibrillation • Oral anticoagulation • Insertable cardiac monitors

What's new?

Key question

How do atrial fibrillation (AF) detection and oral anticoagulation (OAC) rates compare between patients with an insertable cardiac monitor (ICM) vs. external cardiac monitor (ECM) after ischaemic stroke in a real-world population?

Key finding

Insertable cardiac monitor use was associated with a higher probability of AF detection [(hazard ratio (HR) 2.88, 95% confidence interval (CI) (2.31, 3.59)] and OAC initiation (HR 2.91, CI (2.28, 3.72)] compared to patients monitored only with ECM.

Take-home message

In a large real-world cohort of patients with stroke of unknown cause, our results highlight that ICMs provide effective AF detection and have increased OAC therapy, with almost three times more AF and OAC rates compared to ECMs.

Introduction

Cerebral thromboembolism related to atrial fibrillation (AF) is responsible for up to a third of ischaemic strokes, a proportion that increases further with age.[1] Moreover, in up to a quarter of ischaemic strokes or transient ischaemic attacks (TIAs), the cerebral ischaemia constitutes the first clinical documentation of AF, since the arrhythmia was asymptomatic and previously undetected or unrecognized.[2–4] Since AF detection leads to improved secondary prevention strategies, such as prescription of oral anticoagulants (OAC),[5–9] one important step of post-stroke care is AF monitoring whenever cardioembolic mechanism is suspected or the stroke remains 'cryptogenic'.[3,10] A common approach to cardiac monitoring after stroke is telemetry during the initial inpatient stay followed by 24–48 h or extended duration (7–30 days) ambulatory monitoring.[1,10] However, the American Heart Association/American Stroke Association guidelines for the prevention of recurrent stroke recommend long-term rhythm monitoring to detect AF in patients with cryptogenic stroke (IIa recommendation).[11]

Insertable cardiac monitors (ICMs) or cardiac electronic devices with atrial sensing capabilities allow continuous monitoring and have extended the capability to detect AF.[1,12,13] In CRYSTAL AF, a randomized controlled study, that included 441 patients (mean age 62 years) with cryptogenic stroke, long-term monitoring with an ICM was more

effective than conventional follow-up (control) for detecting AF.[14] Clinical practice and patient characteristics in the community often differ from controlled clinical trials; therefore, it is important to study the diagnostic role of ICM in a real-world patient population.

The aim of this study was to compare AF detection and OAC initiation in patients followed with ICM vs. intermittent monitoring systems, in US patients who had been hospitalized with an ischaemic stroke.

Methods

Study design and data sources

We performed a retrospective observational study with Medicare Fee-for-Service (FFS) insurance claims linked with Abbott Laboratories device registration data. Medicare claims included inpatient, outpatient, carrier claims, Part D prescription drug fill records, and Master Beneficiary Summary Files (MBSF). The inpatient and outpatient files contained institutional claims for hospital inpatient services and outpatient services, respectively. The carrier files contained non-institutional provider claims for services rendered in any setting. Each of these files included dates of service, diagnosis, and procedure codes. The prescription drug fill records contain information on medications that were paid under Medicare Part D, which is voluntary insurance coverage for outpatient prescription drugs. Master Beneficiary Summary Files contained information on demographics, birth and death dates, Medicare eligibility, and enrolment. Medicare FFS data were available through 31 December 2020, whilst Part D data were available through 31 December 2019. The Abbott device registration database contained patient-level date of birth, sex, device type, implantation dates, implanting facility, and reason for ICM implant.

The study was conducted as a retrospective analysis of de-identified data. We requested and were granted a full waiver of informed consent and a HIPAA waiver from Western IRB for this study.

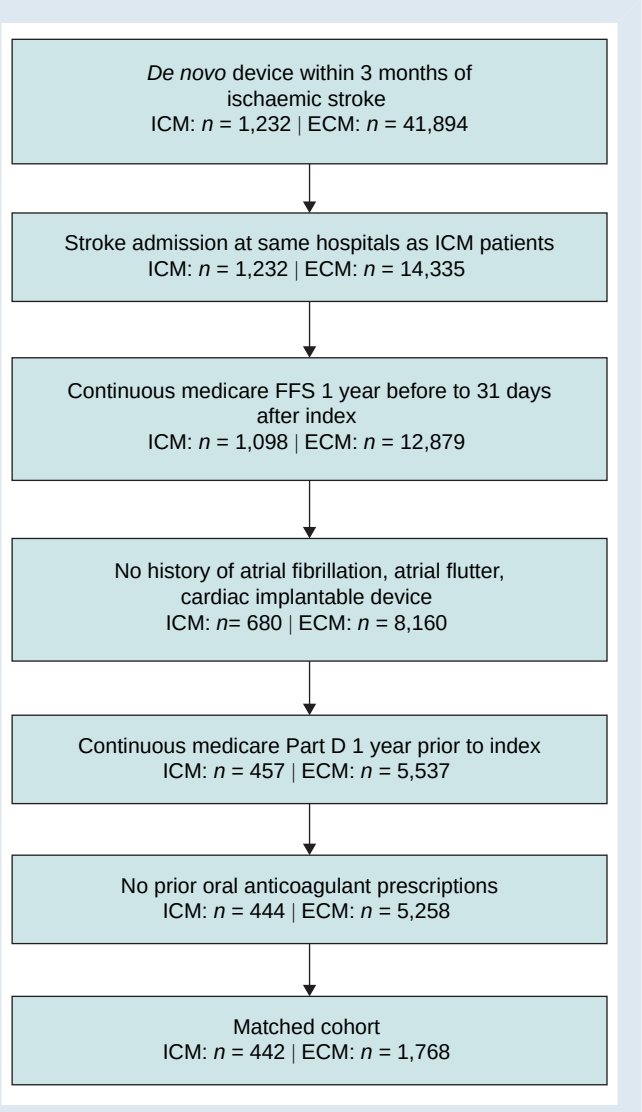


Figure 1 Cohort diagram.
ECM, external cardiac monitor; ICM, insertable cardiac monitor.

Study population

The study population included Medicare FFS beneficiaries who received an ICM (Confirm Rx™ Abbott, USA) or an external cardiac monitor (ECM) between 15 November 2017 and 31 December 2019 and had been hospitalized with an ischaemic stroke in the prior 3 months. Supplementary material online, *Table S1*, in the supplement contains the *International Classification of Diseases Tenth Revision (ICD-10)* codes used to select patients with ischaemic stroke.

The ECM patients (control group) were identified in Medicare claims with procedure codes for Holter monitor, outpatient cardiac telemetry, or memory loop event monitor. The ECM index date was the first post-stroke date with an ECM procedure code.

Patients who received an ICM were identified from Abbott Labs device registration data and Medicare data that were linked using probabilistic linking methods.[15] Briefly, we analysed Medicare claims data to identify patients who received a cardiac insertable electronic device using Current Procedural Terminology® (CPT) Fourth Edition, Healthcare Common Procedure Coding System (HCPCS), and ICD-10 procedure codes. We then linked those Medicare implant records to the Abbott database using patient date of birth, sex, device type, implantation dates, and implanting facility and selected matches based on best agreement between data sources. The ICM index date was the first post-stroke date with an ICM implant (procedure date from Medicare claims). Insertable cardiac monitor patients who first had an ECM post-stroke were placed in the ICM group and not the ECM group.

Patients were included in the study if they had continuous Medicare FFS insurance, Part D insurance enrolment, and no Medicare Advantage enrolment between 12-month pre-index and 31-day post-index. Additionally, ECM patients were only included in the study if they were admitted to a hospital where an ICM patient was also admitted for stroke. As ICD-10 diagnosis codes do not specify whether the stroke was cryptogenic, we further excluded patients whose stroke was unlikely cryptogenic by excluding those with a history of atrial tachyarrhythmias, OAC prescriptions, or cardiac implantable electronic devices (including prior ICMs) at index or in the 12 months prior. Data from Abbott ICM device registration database provided information about the reason for ICM implant for a subset of patients in the ICM cohort. See *Figure 1* for cohort diagram. See Supplementary material online, *Table S1*, in supplement for cohort selection diagnosis and procedure codes.

Outcome measures

The outcomes of interest were AF detection and OAC initiation. We identified AF in claims data when at least one inpatient or two hospital outpatient or physician claims with AF diagnosis codes in the first or second positions on the claim were found. The following ICD-10 AF diagnosis codes were included: I48.0, I48.1, I48.11, I48.19, I48.2, I48.20, I48.21, and I48.91. When comparing AF detection between the groups, we considered AF detected after first ICM implant or after first ECM monitoring. Patients in both groups were censored if they had a new cardiac implant or had an ICM explant. Patients were not censored if they received repeat ECM monitoring, so we continued to follow ECM patients for an AF diagnosis whether they were monitored once or more than once. Available Medicare diagnosis data allowed for patients to be followed for 2 years following the index date; therefore, AF was assessed at 2 years following the index date, and patients were censored after the earliest of the following events: (i) 2 years after the index date, (ii) the end of Medicare FFS claims data availability (31 December 2020), (iii) the date when enrolment in

Medicare FFS ended, (iv) new cardiac implantable electronic device or ICM explant, or (v) death.

Oral anticoagulant initiation is defined as a prescription drug fill record with one of the following drugs: warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban. Available Medicare prescription fill data allowed for patients to be followed for 1.5 years following index date; therefore, OAC was assessed at 1.5 years following the index date, and patients were censored after the earliest of the following events: (i) 1.5 years after the index date, (ii) the end of Part D claims data availability (31 December 2019), (ii) the date when enrolment in Part D ended, (iv) new cardiac implantable electronic device or ICM explant, or (v) death.

Statistical analysis

Insertable cardiac monitor and ECM patients were propensity score matched, with a 1:4 ratio, on baseline characteristics obtained from Medicare claims 12 months prior to index, including demographics (age, sex, and race/ethnicity), comorbidities (listed in *Table 1* and in Supplementary material online, *Table S2*, in supplement with diagnosis codes), stroke hospitalization (length of stay, time between stroke, and index), and index year. Individual components of the CHA_2DS_2-VASc score were used for matching rather than the score itself. Matching was done without replacement using the greedy nearest-neighbour matching method with calliper 0.2. After matching, balance between baseline characteristics was evaluated with the standardized mean difference (SMD) test statistic, where less than 0.10 SMD was considered as achieving balance. For baseline characteristics, categorical variables are presented as frequencies with percentages and continuous variables as means with standard deviations or medians with interquartile range (IQR).

Each outcome was analysed using the Kaplan–Meier method, and log-rank tests were conducted to test for differences in outcomes between the two cardiac monitoring groups. Unadjusted and covariate-adjusted Cox proportional hazard regression models were then run, clustered by the hospital where patients were admitted for stroke. Cox models were evaluated for the proportional hazard assumption. Effect size estimates are provided as hazard ratios (HRs) with 95% confidence intervals (CIs). Sex differences were assessed by the addition of an interaction term to the models. The Kaplan–Meier OAC analysis included all patients in the cohort, regardless of whether they were diagnosed with AF. Descriptive analyses were subsequently conducted to provide OAC rates amongst those who were diagnosed with AF within the OAC follow-up time of 1.5 years. All analyses were conducted in SAS Enterprise Guide version 7.15 (SAS Institute Inc.).

Results

Patient characteristics

A total of 5702 Medicare beneficiaries (ICM, $n = 444$; ECM, $n = 5258$) met inclusion criteria. Differences in baseline characteristics were observed between ICM and ECM patients, as shown in *Table 1*. Insertable cardiac monitor patients had a longer average length of stay during their stroke hospitalization (3.7 vs. 3.1 days), as well as time to index cardiac monitoring after stroke hospitalization (25.9 vs. 22.9 days). Insertable cardiac monitor patients were also more likely to have ischaemic heart disease; patent foramen ovale; cerebrovascular disease, including prior stroke/TIA; and a higher CHA_2DS_2-VASc score. After propensity score matching, all baseline characteristics were balanced (SMDs < 0.10) between ICM and ECM patients. The matched cohort consisted of 2210 Medicare beneficiaries (ICM, $n = 442$; ECM, $n = 1768$) with 53% female, mean age 75 ± 9, CHA_2DS_2-VASc score 4.6 ± 1.6, and stroke hospitalization length of stay 3.5 ± 3.0 days. Both unmatched and matched baseline characteristics are presented in *Table 1*. Data from the Abbott ICM device registration database allowed us to characterize the reason for ICM implant for a subset of patients in the ICM cohort ($N = 161$). Of these patients, 146 (90.7%) had an indication of cryptogenic stroke or suspected atrial fibrillation as the reason for the ICM implant, specifically, 118 (73.3%) were for cryptogenic stroke, and 28 (17.4%) were for suspected atrial fibrillation. The remaining 9.3% of patients had other reasons listed, majority of which were for syncope.

External cardiac monitoring

The types of external cardiac monitoring in the ECM group were as follows: 366 (20.7%) short-term Holter monitors, 473 (26.8%) event monitors, and 929 (52.5%) mobile cardiac telemetry monitors. Amongst ECM patients, there were 176 (10%) who had a repeat ECM within 1 month of index, 77 (4.4%) within 2–3 months of index, and 30 (1.7%) within 4–6 months of index. Over 2 years, 315 (17.8%) of ECM patients had a repeat ECM, with median time to new ECM 30 (4, 109) days. There were 72 (16%) ICM patients who had a post-stroke ECM prior to their ICM implant.

Atrial fibrillation detection

In the AF detection analysis, the median follow-up was 425 (IQR = 141–671) days for ICM and 520 (IQR = 234–730) days for ECM. As detailed in *Figure 2*, the AF detection rate was 33.9% amongst ICM patients compared with 13.3% amongst ECM patients at 2 years ($P < 0.0001$), with an unadjusted HR (95% CI) of 2.84 (2.27, 3.56) and adjusted HR (95% CI) of 2.88 (2.31, 3.59) from the Cox proportional hazard models. There were no significant differences between men and women as indicated by the interaction term in the full model ($P = 0.946$). The proportional hazard assumption was met for the models. The separation of the Kaplan–Meier curves occurred right after index, with AF detection rates of 19.2% amongst ICM patients at 6 months compared to 8.1% amongst ECM patients, 28.1% amongst ICM patients at 12 months compared to 10.4% amongst ECM patients, and 31.0% amongst ICM patients at 18 months compared to 12.2% amongst ECM patients. Log-rank tests indicate all comparisons have $P < 0.0001$. Whilst Medicare claims data do not contain data on AF duration, the Abbott remote monitoring database had AF duration data for a subset of the ICM cohort ($N = 260$). The median (IQR) duration of the maximum daily AF burden in these patients was 1.6 h (0.38, 6.1).

Oral anticoagulant prescriptions

In the OAC prescription analysis, the median follow-up was 241 (IQR = 97–414) days for ICM and 250 (IQR = 84–463) days for ECM. The results of the Kaplan–Meier analysis of OAC prescription fill rate are described in *Table 2*. At 18-month follow-up, the OAC prescription rate, as estimated via Kaplan–Meier analysis, was 35.9% amongst ICM patients and 16.8% amongst ECM patients (log-rank tests $P < 0.0001$), with an unadjusted HR (95% CI) of 2.82 (2.20, 3.62), and adjusted HR (95% CI) of 2.91 (2.28, 3.72) from the Cox proportional hazard models. There were no significant differences between men and women as indicated by the interaction term in the full model ($P = 0.199$). Due to non-proportional hazards, an interaction term between the treatment variable and time was included in the models. Amongst patients who had an AF diagnosis within 1.5 years of index, 59% initiated OACs in both groups; specifically, amongst ECM patients, 35% initiated OAC after AF detection, whilst 24% initiated OAC prior to AF detection, and amongst ICM patients, 47% initiated OAC after AF detection, whilst 12% initiated OAC prior to AF detection.

Death

There were 197 (11.1%) ECM patients and 40 (9.1%) ICM patients who died during the study period. The median follow-up was 583 (IQR = 393–730) days for ICM and 593 (IQR = 374–730) days for ECM.

Stroke/transient ischaemic attack

There were 140 (7.9%) ECM patients and 37 (8.4%) ICM patients who had another stroke or TIA during the study period. The median follow-

Table 1 Characteristics of Medicare beneficiaries using an ICM or an ECM after an ischaemic stroke

	Unmatched ICM n = 444 n (%)	Unmatched ECM n = 5258 n (%)	SMD	Matched ICM n = 442 n (%)	Matched ECM n = 1768 n (%)	SMD
Age, mean (SD)	74.7 (9.0)	75.0 (9.4)	0.029	74.7 (8.5)	74.7 (9.4)	0.010
Female	238 (53.6)	2865 (54.5)	0.018	237 (53.6)	938 (53.1)	0.011
Race/ethnicity						
White	356 (80.2)	4304 (81.9)	0.043	356 (80.5)	1449 (82.0)	0.036
Black	52 (11.7)	491 (9.3)	0.077	51 (11.5)	188 (10.6)	0.029
Hispanic	14 (3.2)	252 (4.8)	0.084	14 (3.2)	55 (3.1)	0.003
Other/unknown	22 (5.0)	211 (4.0)	0.046	21 (4.8)	76 (4.3)	0.022
Index year						
2017	11 (2.5)	262 (5.0)	0.040	11 (2.5)	77 (4.4)	0.020
2018	218 (49.1)	2437 (46.4)		217 (49.1)	822 (46.5)	
2019	215 (48.4)	2559 (48.7)		214 (48.4)	869 (49.2)	
Index to stroke Hospitalization, median (IQR)	−11 (−46, −3)	−14 (−36, −4)	—	−11 (−46, −3)	−17 (−42, −5)	—
Index to stroke Hospitalization, mean (SD)	−25.9 (27.6)	−22.9 (23.0)	0.119	−26.0 (27.6)	−25.7 (24.4)	0.012
Stroke hospitalization LOS, mean (SD)	3.7 (4.1)	3.1 (2.6)	0.168	3.5 (2.7)	3.5 (3.1)	0.006
Comorbidities						
Diabetes	208 (46.9)	2264 (43.1)	0.076	207 (46.8)	829 (46.9)	0.001
Hypertension	424 (95.5)	4954 (94.2)	0.058	422 (95.5)	1701 (96.2)	0.037
Hyperlipidaemia	400 (90.1)	4593 (87.4)	0.087	399 (90.3)	1601 (90.6)	0.010
Ischaemic heart disease	217 (48.9)	2156 (41.0)	0.159	217 (49.1)	891 (50.4)	0.026
Myocardial infarction	78 (17.6)	832 (15.8)	0.047	78 (17.7)	327 (18.5)	0.022
Congestive heart failure	83 (18.7)	960 (18.3)	0.011	83 (18.8)	333 (18.8)	0.001
Valvular heart disease	203 (45.7)	2331 (44.3)	0.028	201 (45.5)	835 (47.2)	0.035
Patent foramen ovale	44 (9.9)	338 (6.4)	0.127	43 (9.7)	174 (9.8)	0.003
Peripheral vascular disease	175 (39.4)	1861 (35.4)	0.083	175 (39.6)	698 (39.5)	0.002
Cerebrovascular disease	132 (29.7)	1140 (21.7)	0.185	130 (29.4)	509 (28.8)	0.014
History of stroke/transient ischaemic attack	94 (21.2)	806 (15.3)	0.152	92 (20.8)	354 (20.0)	0.020
Chronic obstructive pulmonary disease	115 (25.9)	1481 (28.2)	0.051	115 (26.0)	448 (25.3)	0.016
Renal disease	131 (29.5)	1402 (26.7)	0.063	130 (29.4)	521 (29.5)	0.001
Cancer (metastatic or non-metastatic)	68 (15.3)	852 (16.2)	0.024	67 (15.2)	284 (16.1)	0.025
Dementia	48 (10.8)	632 (12.0)	0.038	48 (10.9)	192 (10.9)	0.000
CHA_2DS_2-VASc, mean (SD)	4.61 (1.6)	4.44 (1.5)	0.112	4.61 (1.6)	4.63 (1.6)	0.013

ECM, external cardiac monitor; ICM, insertable cardiac monitor; IQR, interquartile range; LOS, length of stay; SD, standard deviation, SMD, standardized mean difference.

up was 591 (IQR = 376–730) for ECM patients and 577 (IQR = 382–730) for ICM patients.

Discussion

Main findings

In this nationwide study with more than 2000 matched subjects with linked ICM and outcomes data, we found that an ICM monitoring strategy was associated with a much higher rate of AF detection in persons with ischaemic or cardioembolic stroke when compared with external cardiac monitoring. Moreover, we found that ICM monitoring was associated with a much higher rate of initiation of oral anticoagulation. These findings have important implications for the care of patients with stroke because AF may remain undetected even after a first stroke, and this may prevent or delay effective treatment strategies and increase the risk of recurrent stroke.[1]

Comparison with previous findings

In our clinical practice study of older US adults who were hospitalized with ischaemic stroke, which was cryptogenic in about 90% of patients, ICM patients were almost three times more likely to be diagnosed with AF and to be prescribed OAC compared to ECM patients. In particular, the AF detection rate was 33.9% amongst ICM patients compared with 13.3% amongst ECM patients at 2 years.

Only a small number of studies have evaluated the clinical impact of ICM usage in cryptogenic stroke patients treated in clinical practice.[16–18] Ziegler *et al.*[16] evaluated a cohort of 1247 US patients

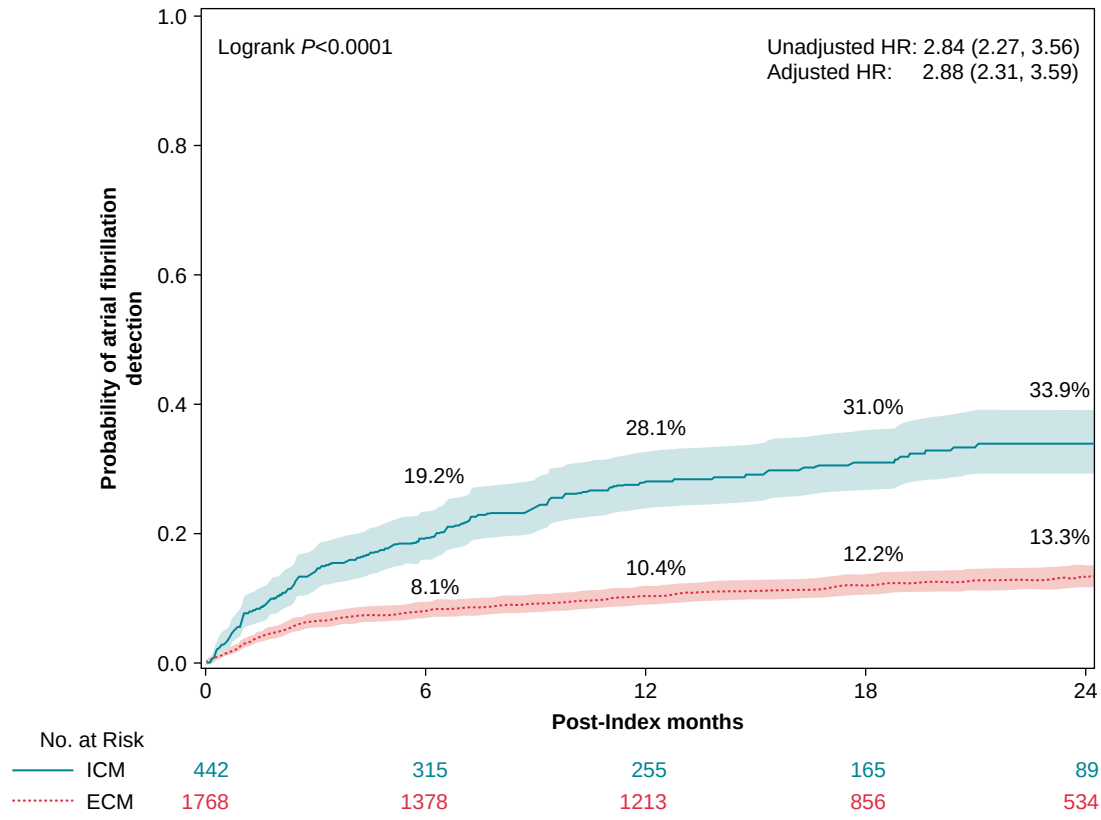


Figure 2 Two-year atrial fibrillation incident rates by cardiac monitor method, ICM (solid line) and ECM (dashed line). Rates were estimated using the Kaplan–Meier method. Hazard ratios and 95% CIs estimated by Cox proportional hazard models are also shown. ECM, external cardiac monitor; ICM, insertable cardiac monitor.

with cryptogenic stroke and reported an AF detection rate of 12.2% at 6 months and 21.5% at 2 years. Ungar *et al.*[17] followed 334 cryptogenic stroke Italian patients with a mean age of 67 ± 12 years. In 62% of these patients, short-term Holter monitoring was performed before ICM implant. During a median follow-up of 23.6 months, subclinical AF was detected in 22.0%, 24.1%, and 31.5% at 6, 12, and 24 months, respectively, after ICM implantation, similar to the findings of our study. Furthermore, AF was asymptomatic in 88.1% of their patients.

In our clinical practice study, ICM patients were almost three times more likely to be prescribed OAC compared to ECM patients. In particular, at 18 months, the OAC prescription rate was 35.9% amongst ICM patients and 16.8% amongst ECM patients. Yaghi *et al.*[18] performed an analysis on 12 994 US patients with incident hospitalization for cryptogenic stroke, identified in the Optum® claims database with 1949 ICM patients and 11 045 ECM patients. This study reported that ICM provided faster AF diagnosis compared with ECM and OAC drugs were prescribed in 30% of ICM patients vs. 19% of ECM patients at 18 months.

Table 2 Oral anticoagulant prescription rate by cardiac monitoring method amongst Medicare patients hospitalized with ischaemic stroke, 2017–2019

Follow-up (months)	ICM % (95% CI)	ECM % (95% CI)
6	13.6 (10.5–17.5)	11.2 (9.7–12.9)
12	30.9 (25.7–36.8)	14.7 (12.9–16.8)
18	35.9 (30.1–42.4)	16.8 (14.7–19.2)

The table shows 1.5-year oral anticoagulant prescription rates and 95% CIs by cardiac monitoring method, ICM and ECM. Rates were estimated using the Kaplan–Meier method.
ECM, external cardiac monitor; ICM, insertable cardiac monitor.

The results from our analysis extend these observations[16–18] and highlight the clinical implications of enhanced AF detection capabilities that ICM can obtain in an older, sicker patient population with ischaemic stroke. Other studies, both real-world and clinical trial, were mostly focused on younger and healthier patient populations; for example, the patients in our study had higher CHA_2DS_2-VASc scores and were ~13 years older than those enrolled in the CRYSTAL AF clinical trial (75 vs. 62 years).[14] Age is an important factor since AF, including long-duration AF and asymptomatic AF, is more frequent with older age.[19,20] Older patients who experienced a stroke could substantially benefit from reduction of stroke recurrences that anticoagulation may allow if an associated AF is detected. Patient age also emerged as independently associated with increased AF detection through an ICM in a secondary analysis of the CRYSTAL AF trial.[21]

There is substantial uncertainty and variability in the interpretation of so-called 'subclinical AF', but usually after stroke, the threshold for prescribing OAC is low, even if an AF episode lasting only a few minutes is detected.[22,23] In the CRYSTAL AF trial,[24] 92% of patients with detected AF were prescribed OAC, and AF duration influenced OAC

prescription; all patients with at least one long AF episode (>1 h) were prescribed OAC therapy compared with 70% of patients with only brief episodes (<1 h). The median duration of the maximum daily AF burden in a subset of our ICM cohort was 1.6 h. Our study was based on AF diagnosis codes and therefore relates to clinical AF detected by ICM or ECM. In both groups, 59% of patients with an AF diagnosis had an OAC prescription. This is consistent with other US-based studies on OAC underutilization in patients with AF, which may be related to various reasons[25–27], whilst rates of OAC initiation in European patient populations tend to be higher.[27–29] It is noteworthy that in some cases, prescription of OAC was done even before AF diagnosis, which could be due to clinical judgement or an artefact of using administrative data. In fact, other real-world studies[30,31] were designed to look for OAC before and after AF diagnosis as well. Using Medicare claims data, Norby *et al.* defined first OAC as OAC found in claims 30 days prior to any time after first AF diagnosis. Using commercial claims data, O'Neal *et al.* defined OAC as OAC found in claims 3 months prior to 6 months after first AF diagnosis.

Clinical implications

In a large real-world cohort of patients with a stroke of unknown cause, our results highlight that ICMs lead to increased rates of AF detection and increased use of OAC therapy by approximately three times compared to ECMs. Improved detection of AF may translate into improved treatment and consequently reduced risk of stroke and death. Indeed in the study recently published by Yaghi *et al.*,[18] ICM use was associated with a significantly reduced risk of death with HR = 0.70, CI 0.55–0.89. Also in the meta-analysis performed by Tsivgoulis *et al.*[32] ICM use, compared with conventional monitoring in cryptogenic stroke patients, was associated with increased AF detection yield, higher OAC initiation, and decreased risk of recurrent stroke with ICM. Our data do not show a significant reduction of death in ICM patients vs. ECM patients, likely due to the sample size and limited follow-up length for studying rare events such as death.

The benefit of continuous vs. intermittent AF monitoring is of particular clinical relevance when AF is infrequent, paroxysmal, and asymptomatic.[33–38] Detection of AF in patients with cryptogenic stroke and subsequent treatment with OAC is also important because silent brain infarcts have an impact on cognitive function in AF patients.[39] Moreover, continuous rhythm monitoring enables an improved characterization of diverse AF patterns and their longitudinal changes, which may bring attention to progressive remodelling of the atrial substrate or worsening underlying diseases.[40–44]

Strengths and limitations

We performed a retrospective analysis of a large real-world database of patients with a stroke of unknown cause. The impact of monitoring strategies for AF detection in cryptogenic stroke has mostly been evaluated in randomized controlled trials (RCTs),[14,21,24,45] which are performed in selected patient populations, with variable risk of AF detection,[33] and often with important differences compared with clinical practice.[46] Compared with prior studies, our results may be more generalizable to an older, sicker real-world patient population that more closely reflects the population affected by AF.

Whilst the use of observational data has many advantages, there are also important limitations that must be kept in mind. Initially there were important differences in patient characteristics between the two groups; we therefore used propensity score matching and further covariate adjustment to balance patient characteristics. Specifically, ICM patients had higher rates of cardiovascular diseases and higher CHA_2DS_2-VASc scores prior to matching. We attempted to minimize confounding with propensity score matching and further adjusting models for covariates and by limiting ECM patients to those who were admitted to the same hospitals as ICM patients for stroke. However, we cannot exclude the possibility that residual confounding impacted our results. Additionally, there are currently no specific diagnosis codes for cryptogenic stroke. We have minimized this limitation by excluding patients who likely did not have cryptogenic stroke, such as patients with a history of atrial tachyarrhythmias, implantable cardiac electronic devices, and OAC prescriptions, and our ICM registration data indicate that in a subset of the ICM cohort with data on reason for ICM implant, majority had the reason of cryptogenic stroke. We also could not adjust for stroke severity since validated data on this measure were not available in insurance claims; however, we adjusted for hospital length of stay, which is related to stroke severity. The follow-up time in our study differed according to the study endpoint due to differences in censoring, e.g. the follow-up for OAC was shorter due to a lag in data availability for Medicare Part D compared to Medicare FFS. We also could not evaluate recurrent stroke and other clinical outcomes due to low statistical power. The study population was limited to US patients with Medicare FFS insurance and may not be generalizable to younger patients. With this regard, it is noteworthy that there is an important heterogeneity of reimbursement practices across Europe, and some revision and update of related policies would be desirable, also taking into account innovative approaches.[47–49]

Conclusions

In a nationwide cohort of older patients with ischaemic stroke, we compared different cardiac monitoring strategies to detect AF as a potential cause of stroke. Long-term monitoring through an ICM yielded more frequent and timely AF detection rates and OAC prescription fills compared to short-term ECMs. Patients monitored with an insertable monitor were almost three times more likely to be diagnosed with AF and to be prescribed OAC compared to patients monitored with an external monitor.

Supplementary material

Supplementary material is available at *Europace* online.

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Conflict of interest: G.B. received small speaker's fees from Abbott, Bayer, Boston, Boehringer, Daiichi Sankyo, Janssen, and Sanofi, outside of the submitted work. A.A, is a consultant to Abbott, Boston Scientific, Cairdac, EP Solutions, Hylomorph, Medtronic, and XSpline; has received speaker fees from Boston Scientific, Medtronic, Microport CRM, and Philips; participates in clinical trials sponsored by Abbott, Boston Scientific, EPD-Philips, EP Solutions, Medtronic, Philips, and XSpline; and holds intellectual properties with Boston Scientific, Biosense Webster, and Microport CRM. G.L.B. has received speaker fees (small amount) from Abbott, Biotronik, Boston Scientific, Medtronic, and Microport CRM. J.P.P. is supported by R01AG074185 from the National Institutes of Aging. He also receives grants from Abbott, the American Heart Association, the Association for the Advancement of Medical Instrumentation, Bayer, Boston Scientific, iRhythm, and Philips and serves as a consultant to Abbott, Abbvie, ARCA biopharma, Bayer, Boston Scientific, Element Science, LivaNova, Medtronic, Milestone, ElectroPhysiology Frontiers, Sanofi, Philips, and Up-to-Date. J.M.J., G.J.R., A.G., and Y.N. are employed by Abbott.

Data availability

Centers for Medicare & Medicaid Services data can be requested under an approved research protocol via ResDAC (www.resdac.org). Restrictions apply to the availability of data generated and analysed for this study to preserve patient confidentiality. Data were used under a data use agreement. Requests to access these data sets should be directed to ResDAC, resdac@umn.edu.

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