Received: 23 July 2022 | Revised: 9 October 2022 | Accepted: 25 October 2022

DOI: 10.1111/jce.15744

ORIGINAL ARTICLES

WILEY

Atrial fibrillation detection using insertable cardiac monitor after stroke: A real-world cohort study

Jean J. Noubiap MD, MMed[1,2] | Gijo Thomas PhD[1] | Melissa E. Middeldorp PhD[1,2] | John L. Fitzgerald MBBS[1,2] | Curtis Harper CCDS[3] | Prashanthan Sanders MBBS, PhD[1,2]

[1]Centre for Heart Rhythm Disorders, University of Adelaide, Adelaide, Australia

[2]Department of Cardiology, Royal Adelaide Hospital, Adelaide, Australia

[3]Pacemate, Bradenton, Florida, USA

Correspondence

Prashanthan Sanders, MBBS, PhD, Department of Cardiology, Centre for Heart Rhythm Disorders, Royal Adelaide Hospital, Adelaide, SA 5000, Australia.
Email: prash.sanders@adelaide.edu.au

Disclosure Drs Jean J. Noubiap and John L. Fitzgerald are supported by a Postgraduate Scholarship from the University of Adelaide; Dr Melissa E. Middeldorp is supported by a Postdoctoral Fellowship from the University of Adelaide; Dr Prashanthan Sanders is supported by a Practitioner Fellowship from the National Health and Medical Research Council and also by the National Heart Foundation of Australia, reports having served on the advisory board of Medtronic, Abbott Medical, Boston Scientific, CathRx and PaceMate, and reports that the University of Adelaide has received on his behalf research funding, lecture and/or consulting fees from Medtronic, Abbott Medical, Boston Scientific and Microport; and Mr Curtis Harper is employed by Pacemate. Other author: No disclosure.

Abstract

Objective: This study aimed to report the real-world atrial fibrillation (AF) diagnostic yield of the implantable cardiac monitor (ICM) in patients with stroke or transient ischemic attack (TIA), and compare it to patients with an ICM for unexplained syncope.

Methods: We used patient data from device clinics across the United States of America with ICM remote monitoring via PaceMate™, implanted for stroke or TIA, and unexplained syncope. Patients with known AF or atrial flutter were excluded. The outcome was AF lasting ≥2 min, adjudicated by International Board of Heart Rhythm Examiners certified cardiac device specialists.

Results: We included a total of 2469 patients, 51.1% with stroke or TIA (mean age: 69.7 [SD: 12.2] years, 41.1% female) and 48.9% with syncope (mean age: 67.0 [SD: 17.1] years, 59.4% female). The cumulative AF detection rate in patients with stroke or TIA was 5.5%, 8.9%, and 14.0% at 12, 24, and 36 months, respectively. The median episode duration was 73 (interquartile range: 10–456) min, ranging from 2 min to 40.9 days, with 52.3%, 28.6%, and 4.4% of episodes lasting at least 1, 6, and 24 h, respectively. AF detection was increased by age (adjusted hazard ratio [for every 1-year increase]: 1.024, 95% confidence interval: 1.008–1.040; $p = .003$), but was not influenced by sex ($p = .089$). For comparison, the cumulative detection rate at 12, 24, and 36 months were, respectively, 2.4%, 5.2%, and 7.4% in patients with syncope.

Conclusion: Patients with stroke or TIA have a higher rate of AF detection. However, this real-world study shows significantly lower AF detection rates than what has been previously reported.

KEYWORDS

atrial fibrillation, cryptogenic stroke, implantable cardiac monitor, internal loop recorder, real-world, transient ischemic attack

1 | INTRODUCTION

Atrial fibrillation (AF) is a major cause of ischemic stroke.[1] AF-related cardioembolism accounts for up to one-third of all ischemic strokes,[1] and AF increases the risk of recurrent ischemic stroke by 15% during the first year after stroke. Furthermore, the case fatality and disability are worse in ischemic strokes due to AF compared to those from other causes.[2,3] There is also a substantial fraction of ischemic strokes for which the likely cause cannot be identified by routine investigations.[2] A proportion of these embolic strokes of undetermined source could be due to paroxysmal, asymptomatic AF.[1] Searching for AF poststroke is critical because recurrent AF-related stroke can largely be prevented by oral anticoagulation.[1]

The rates of AF detection poststroke vary significantly depending on the population, the monitoring strategy, the length of monitoring, and the duration cutoff to define AF episodes.[1] Insertable cardiac monitors (ICM) have become an important tool for AF diagnosis after stroke.[1] The seminal cryptogenic stroke and underlying AF (CRYSTAL AF) trial revealed significantly increased AF detection with prolonged continuous cardiac monitoring with ICM over standard-of-care monitoring in patients with cryptogenic stroke.[4] In this trial, the rate of AF detection was 12.4% at 12 months and 30.0% at 36 months of monitoring using ICM.[4] These detection rates in clinical trials might be different in real-world settings. In a real-world cohort of patients receiving prolonged cardiac monitoring with ICM, the current study aimed to report the AF diagnostic yield in patients undergoing monitoring after stroke and to compare it to the yield in patients with ICM for unexplained syncope.

2 | METHODS

2.1 | Study design and data source

This is an investigator-initiated retrospective multicenter observational cohort study including patients from device clinics across multiple states in the United States of America (Alabama, Colorado, Illinois, Kansas, Kentucky, Louisiana, Maine, New Jersey, Ohio, Oklahoma, South Carolina, Texas, and Virginia), receiving remote monitoring using ICM via PaceMate™, a vendor-neutral digital technology software. Data were obtained from PaceMate LIVE™, a software system that automatically integrates all remote monitoring transmissions from multiple device vendor platforms and streamlines them into a single user interface.

2.2 | Study population and diagnosis ascertainment

We included all patients receiving ICM for stroke or transient ischemic attack (TIA) (main group), and unexplained syncope (comparison group). Diagnoses were identified through the International Classification of Diseases, 10th revision codes. Patients with a known history of AF or atrial flutter were excluded. We collected data on age, sex, and monitoring information including the date of ICM implantation, the date of AF detection, and the duration of the AF episode.

The study outcome was AF defined as an episode of irregular rhythm without detectable P waves, lasting at least 2 min, detected by the ICM and adjudicated by a certified cardiac technician.

2.3 | Statistical analysis

Categorical variables were expressed as frequencies and percentages while continuous variables were expressed as mean with standard deviation (SD) or median with interquartile range (IQR) as appropriate. AF detection rates were assessed using the Kaplan–Meier estimator. In addition to detection rates based on the cutoff duration of 2 min for an AF episode, rates were also determined for cutoffs of 6, 30, and 60 min. Cox regression analysis was used to evaluate the impact of age and sex on the AF detection rate. A $p < .05$ was considered significant. All analyses were performed using IBM SPSS Statistics version 27.0 and STATA 16.1.

3 | RESULTS

3.1 | Sociodemographic and indications for ICM

We included a total of 2469 patients. The indication for ICM was stroke or TIA in 51.1% of them ($n = 1262$; 19.3% with TIA), and unexplained syncope in 48.9% ($n = 1207$). Those with ICM for stroke or TIA had a mean age of 69.7 (SD: 12.2) years, with 41.1% being females; whereas those with ICM for unexplained syncope had a mean age of 67.0 (SD: 17.1) years, with 59.4% being females.

3.2 | AF detection rates

In this study with a median follow-up of 26.0 (IQR: 13–29.3) months, AF (≥2 min) was detected in 128 (10.1%) patients with stroke or TIA. The cumulative AF detection rate was 5.5% (95% confidence interval: 4.3–7.0) at 12 months, 8.9% (95% CI: 7.2–10.9) at 24 months, and 14.0% (95% CI: 11.6–17.0) at 36 months (Figure 1). The median episode duration was 73 min (IQR: 10–456), ranging from 2 min to 40.9 days, with 52.3%, 28.6%, and 4.4% of episodes lasting at least 1 h, 6 h, and 24 h, respectively. For comparison, the cumulative detection rate at 12, 24, and 36 months were, respectively, 2.4% (95% CI: 1.7–3.5), 5.2% (95% CI: 3.9–6.8), and 7.4% (95% CI: 5.7–9.6) in patients with unexplained syncope (Figure 1).

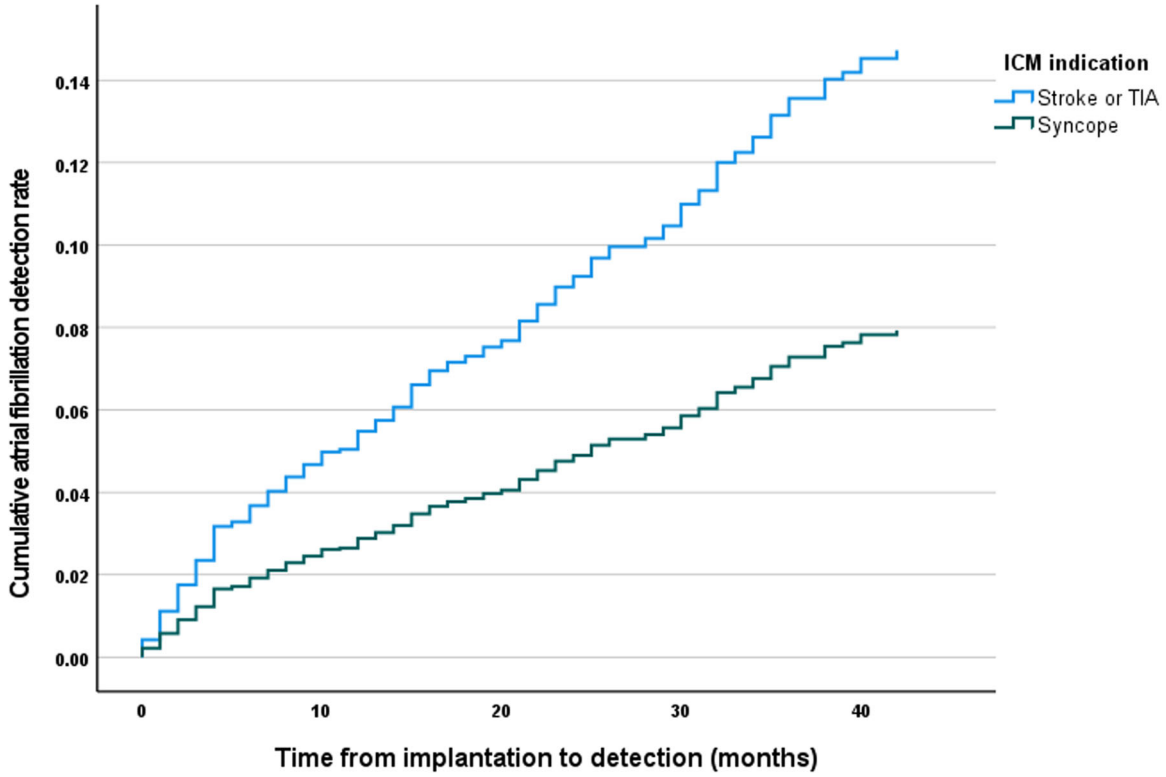

FIGURE 1 Cumulative atrial fibrillation detection rates in patients with stroke or transient ischemic attack and unexplained syncope

Factors	Univariable Cox regression		Multivariable Cox regression	
	Crude hazard ratio (95% CI)	*p* Value	Adjusted hazard ratio (95% CI)	*p* Value
Age (years)	1.021 (1.006–1.037)	.007	1.024 (1.008–1.040)	.003
Male gender	1.636 (0.846–3.162)	.143	1.777 (0.917–3.443)	.089

Abbreviation: CI, confidence interval.

TABLE 1 Association of age and sex with atrial fibrillation detection in patients with stroke or transient ischemic attack

3.3 | Impact of age and sex on AF detection

In patients with stroke or TIA, AF detection was increased by age (adjusted hazard ratio [for every 1-year increase]: 1.024, 95% CI: 1.008–1.040; $p = .003$), but was not influenced by sex ($p = .089$) (Table 1).

3.4 | Impact of AF duration cutoff on detection rates

Using different cutoff durations to define an AF episode resulted in different AF detection rates: 5.5% (≥2 min), 4.4% (≥6 min), 3.5% (≥30 min), and 3.0% (≥60 min) at 12 months; and 14.0% (≥ 2 min), 12.2% (≥6 min), 8.7% (≥30 min), and 7.5% (≥60 min) at 36 months (Figure 2).

4 | DISCUSSION

The main purpose of this study was to report the AF diagnostic yield of ICM in patients with stroke. In this large real-world cohort, we observed a cumulative AF detection rate of 14% at 36 months. The detection yield increased with age but did not differ between sexes. The AF diagnostic yield in patients with stroke in our study is lower than that reported in the landmark CRYSTAL AF trial, in which the rate of AF detection was 12.4% at 12 months, and 30.0% at 36 months of monitoring using ICM in patients with cryptogenic stroke.[4] The AF detection rate in our study is also lower than that of most previous studies using ICM in patients with cryptogenic stroke or embolic stroke of undetermined source.[5] However, a similar detection rate to ours has been previously suggested. In a small sample of patients ($n = 145$) who had ICM for cryptogenic stroke between 2014 and 2018 at New York University Langone Health,[6] over a mean follow-up of 28 months, AF

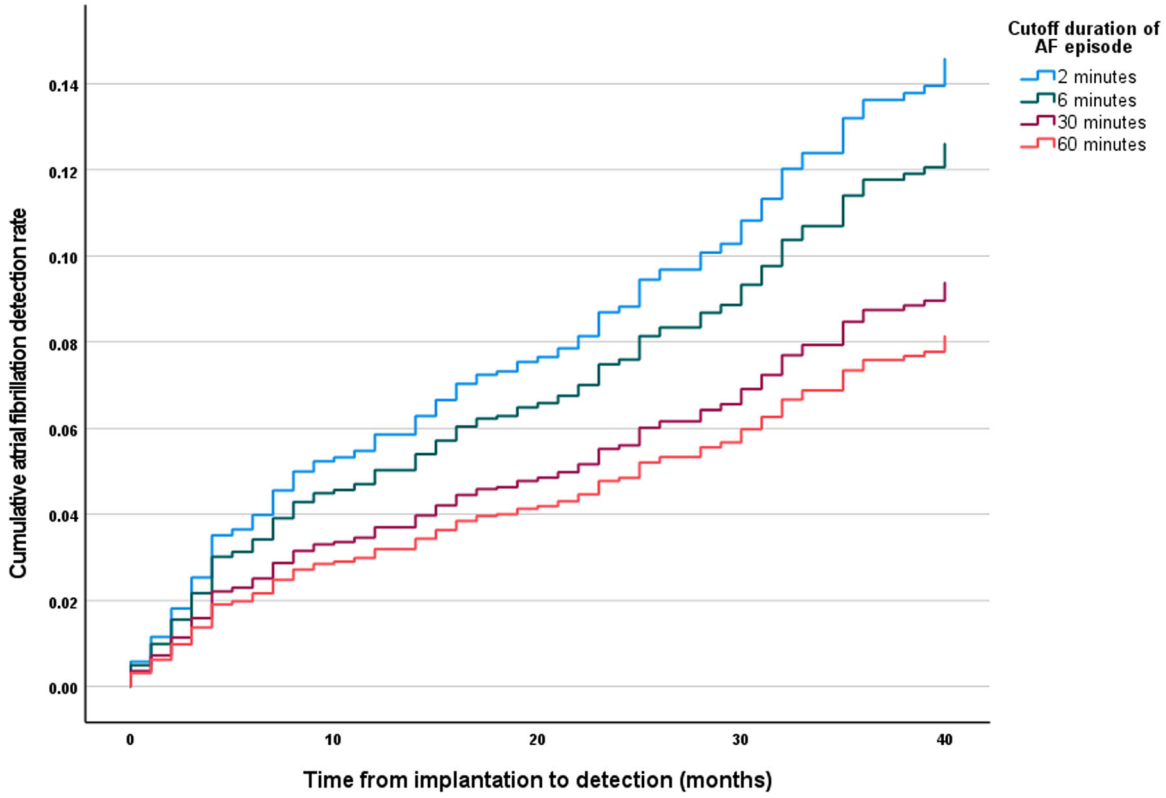

FIGURE 2 Cumulative atrial fibrillation detection rates in patients with stroke or transient ischemic attack according to different cutoff durations

was diagnosed in 12% of patients, with a detection rate being 7.6% at 12 months, 9% at 24 months, and 11.7% at 36 months.[6]

There are a few plausible explanations for the lower detection rates in our study. We used a cutoff of 120 s to define AF due to the reliability of detection documented by the Reveal Linq device. Although the CRYSTAL-AF study used the same device in terms of reliability, the study reports including AF episodes >30 s.[4] With a 30 s cutoff definition, our AF detection yield might have been higher. In fact, we observed increasing AF detection rates with lower cutoffs (from 60 to 2 min). Furthermore, the proportion of patients with TIA (19.3%), as the indication for monitoring in our study, was higher than what has been reported in several previous studies. For instance, this proportion was 9.5% in the CRYSTAL AF trial.[4] It has been shown that AF is more common in patients with ischemic stroke than in those with TIA.[7] In the absence of detailed clinical information, it was not possible for us to investigate the association between the clinical profile of patients and AF detection rates.

According to pooled data from previous studies, most cases of AF (about half) are detected in the first 6 months after ICM implantation following cryptogenic stroke.[5] We observed a different pattern in our study in which most cases of AF were detected more than 6 months after implantation. It is uncertain whether AF detected much later is responsible for the index stroke. These cases of AF might represent new-onset AF resulting from increasing age and the impact of co-morbidities.[1] Indeed, in our study AF was also detected over time in patients with ICM for unexplained syncope, although the detection rate was almost half the rate observed in patients with stroke or TIA. Further studies are needed to determine the clinical relevance of such cases of screen-detected AF, especially in view of the findings of the LOOP study in which ICM screening followed by anticoagulation initiation in cases with detected AF (duration ≥6 min) did not significantly reduce the risk of stroke or systemic embolism in individuals at high risk of stroke.[8]

Our finding of higher AF detection with increasing age is consistent with what has been previously reported in patients with cryptogenic stroke or embolic stroke of undetermined source receiving prolonged continuous cardiac monitoring.[5] We found no association between sex and AF detection. A recent systematic review and meta-analysis showed an association of the female sex with AF detection in patients with cryptogenic stroke.[5] However, this finding emerged from univariable pooled analysis that did not account for potential confounders, and the association between the female sex and AF detection was driven by one study.[5] In general, most studies revealed that sex does not influence AF detection in this population.[5]

Our study has some limitations. First, because this study was retrospective and based on data from a real-world remote monitoring registry using diagnosis codes, there is a potential for selection bias and ascertainment bias. Second, information on the time between stroke and ICM implantation, investigations were done before ICM implantation, and clinical characteristics were not available. Such information would have helped understand the AF detection rates observed in our study. Nevertheless, our study is one of the largest

real-world cohorts of patients monitored with ICM after ischemic stroke.[5]

5 | CONCLUSION

This large real-world study shows lower AF detection rates in patients with ischemic stroke compared to what has been reported in most previous studies. The detection of AF increases with age but does not seem to be influenced by sex.

AUTHOR CONTRIBUTIONS

Conception and design: Jean J. Noubiap, Melissa E. Middeldorp, and Prashanthan Sanders. *Access to data*: Jean J. Noubiap, Curtis Harper, and Prashanthan Sanders. *Data analysis*: Jean J. Noubiap and Gijo Thomas. *Data interpretation*: Jean J. Noubiap and Gijo Thomas. *Manuscript drafting*: Jean J. Noubiap. *Manuscript revision*: Jean J. Noubiap, Gijo Thomas, Melissa E. Middeldorp, John L. Fitzgerald, Curtis Harper, and Prashanthan Sanders. *Approval of the final manuscript*: All authors.

ACKNOWLEDGMENT

Open access publishing facilitated by The University of Adelaide, as part of the Wiley - The University of Adelaide agreement via the Council of Australian University Librarians.

ETHICS STATEMENT

This study was approved by the Human Research Ethics Committee of the Central Adelaide Local Health Network, Adelaide, Australia.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Jean J. Noubiap http://orcid.org/0000-0002-7722-9757
Melissa E. Middeldorp http://orcid.org/0000-0002-4106-9771
Prashanthan Sanders http://orcid.org/0000-0003-3803-8429

REFERENCES

1. Schnabel RB, Haeusler KG, Healey JS, et al. Searching for atrial fibrillation poststroke: a white paper of the AF-SCREEN International Collaboration. *Circulation*. 2019;140(22):1834-1850.
2. Li L, Yiin GS, Geraghty OC, et al. Incidence, outcome, risk factors, and long-term prognosis of cryptogenic transient ischaemic attack and ischaemic stroke: a population-based study. *Lancet Neurol*. 2015;14(9):903-913.
3. Kaarisalo MM, Immonen-Räihä P, Marttila RJ, et al. Atrial fibrillation and stroke. Mortality and causes of death after the first acute ischemic stroke. *Stroke*. 1997;28(2):311-315.
4. Sanna T, Diener HC, Passman RS, et al. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med*. 2014;370(26):2478-2486.
5. Noubiap JJ, Agbaedeng TA, Kamtchum-Tatuene J, et al. Rhythm monitoring strategies for atrial fibrillation detection in patients with cryptogenic stroke: a systematic review and meta-analysis. *Int J Cardiol Heart Vasc*. 2021;34:100780.
6. Chorin E, Peterson C, Kogan E, et al. Comparison of the effect of atrial fibrillation detection algorithms in patients with cryptogenic stroke using implantable loop recorders. *Am J Cardiol*. 2020;129:25-29.
7. Buchwald F, Norrving B, Petersson J. Atrial fibrillation in transient ischemic attack versus ischemic. *Stroke*. 2016;47(10):2456-2461.
8. Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (the LOOP study): a randomised controlled trial. *Lancet*. 2021;398:1507-1516.

How to cite this article: Noubiap JJ, Thomas G, Middeldorp ME, Fitzgerald JL, Harper C, Sanders P. Atrial fibrillation detection using insertable cardiac monitor after stroke: a real-world cohort study. *J Cardiovasc Electrophysiol*. 2023;34:142-146. doi:10.1111/jce.15744