



Medicare claims–based evaluation of atrial fibrillation within implantable cardiac monitor patients with cryptogenic stroke

Steven Mullane¹ · Camden Harrell¹ · Nikolaos Tsitiridis² · Gaurav Upadhyay³ · Jim W. Cheung⁴ · David Hayes¹

Received: 26 July 2023 / Accepted: 21 August 2023 / Published online: 29 August 2023
© The Author(s) 2023

1 Background

In patients with cryptogenic stroke (CS), the risk of recurrent stroke is high, making early detection and treatment essential [1]. Implantable cardiac monitors (ICMs) are an important diagnostic tool that can detect arrhythmias that may have gone undetected during routine electrocardiogram monitoring (ECG) and are increasingly being used to diagnose arrhythmias in patients with CS [2]. Studies have shown that the use of ICMs improves the detection rate of atrial fibrillation (AF) compared to standard ECG monitoring [2].

To help identify patients who are at increased risk of recurrent stroke and may benefit from anticoagulation therapy, the European Society of Cardiology (ESC) guidelines for the management of AF recommend the use of ICMs in patients with CS to detect AF [3]. Additionally, the American Heart Association/American Stroke Association (AHA/ASA) guidelines have long-term cardiac monitoring for patients with CS as a Class IIa recommendation when external monitoring is inconclusive [4].

The UK's National Institute for Health and Care Excellence (NICE) guidance, however, does not currently recommend the use of certain ICMs to help detect AF after CS due to lack of research [5]. Therefore, this analysis aims to further evaluate diagnostic yield of AF for CS patients with a BIOTRONIK ICM.

2 Methods

2.1 Data sources and patient identification

This analysis utilized the CERTITUDE real-world database, which has been described previously [6], to retrospectively investigate Medicare Fee-For-Service (FFS) beneficiary patients with BIOMONITOR III/III_m (BIOMONITOR) and indication related to CS with no prior history of AF. Indication of CS was identified from BIOTRONIK Home Monitoring (HM) data. Patients with prior AF diagnosis identified in Medicare FFS administrative claims data at time of implant were excluded from the analysis.

2.2 Identification of atrial fibrillation

The primary outcome of interest was the diagnosis of AF following the implantation of BIOMONITOR. To identify cases of AF, non-overlapping Medicare FFS inpatient, outpatient, or carrier claims were examined for primary or secondary diagnosis codes indicative of AF using claims as established in Center for Medicare and Medicaid Services (CMS) Chronic Conditions Data Warehouse validated algorithms [7]. Patients with such codes were considered to have a diagnosis of AF. Additionally, daily maximum device-detected AF burden was also evaluated from transmitted HM data.

2.3 Comparison to CRYSTAL AF trial

The results obtained from the study were compared to the historical reported results of the CRYSTAL AF trial [2]. The comparison aimed to assess the agreement between the real-world data from the CERTITUDE database and the findings from this clinical trial. The proportion of patients diagnosed with AF following implantation was calculated based on the patients identified as having AF in Medicare claims data. The comparison to the CRYSTAL AF study was performed using binomial proportion test to determine the level of agreement.

✉ Steven Mullane
steven.mullane@biotronik.com

¹ BIOTRONIK, Inc., 6024 Jean Road, Lake Oswego, OR 97035, USA

² BIOTRONIK SE & Co. KG, Woermannkehe 1, 12359 Berlin, Germany

³ Department of Medicine, Section of Cardiology, Center for Arrhythmia Care, The University of Chicago Medicine, Pritzker School of Medicine, Chicago, IL, USA

⁴ Department of Medicine, Weill Cornell Medicine–New York Presbyterian Hospital, New York, NY, USA

3 Results

A total of 247 eligible patients were identified in the CERTITUDE database meeting eligibility requirements. By 12 months, 17.4% (43 of 247) patients had been diagnosed with AF as identified in CMS claims (95% CI of 12.9%, 22.7%) and an incidence rate of 0.341 events/subject-year with a total follow-up time of 125.9 years. Cumulative incidence of AF is shown in Fig. 1. From HM device data, the maximum atrial burden percentage of the 43 patients diagnosed with AF was 18.4% \pm 26.7%.

3.1 Comparison to CRYSTAL AF trial

The BIOMONITOR cohort demonstrated a significantly higher proportion of AF diagnosis at 12 months compared to the 1.9% (4/213) of patients with AF diagnosis in the non-ICM cohort from the CRYSTAL AF trial ($p < 0.001$). No significant difference ($p = 0.0826$) in proportion of AF diagnosis was found between BIOMONITOR and the CRYSTAL AF trial ICM cohort of 13.6% (29/213) patients with AF diagnosis at 12 months.

4 Discussion

In this retrospective real-world data analysis, we found 17.4% of CS patients were diagnosed with AF within 12 months following ICM implant. The high prevalence of AF in patients with CS has been well-documented in previous studies, such as the CRYSTAL AF trial, which was a landmark study that demonstrated the value of ICMs in this patient population [2]. Our real-world data findings align with the results of this study, further supporting the

effectiveness of ICMs, such as the BIOMONITOR, in identifying AF in CS patients.

While not evaluated in this analysis, patient characteristics and comorbidities may influence the rate of AF diagnosis. Future studies could explore the impact of patient characteristics on AF detection rates to better understand the patient populations that may benefit the most from ICM monitoring.

Overall, the use of ICMs in patients with CS is a valuable diagnostic tool and has gained recognition in clinical practice and by ESC and AHA/ASA [4, 5] to help identify underlying arrhythmias that may have gone undiagnosed and help guide appropriate therapy to reduce the risk of recurrent stroke. Our analysis provides further evidence to support these guidelines.

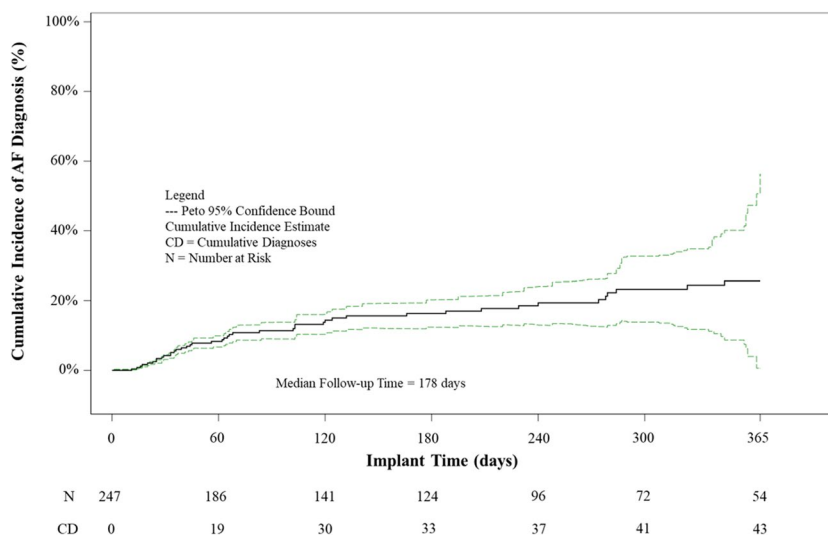
4.1 Limitations

This analysis relied on patients with Medicare FFS coverage, which may not be fully representative of the general population. To minimize possibility of false-positive detections from ICMs, we focused on clinical diagnosis of AF within CMS claims data instead of the device-detected atrial burden or atrial episodes, but the accuracy of the diagnosis of AF in claims is subject to potential coding errors.

5 Conclusion

Our study highlights the importance of ICMs in the diagnosis of AF in patients with CS indication. The detection rate of 17.4% aligns with prior studies, including the landmark CRYSTAL AF trial, and underscores the clinical significance of ICMs, such as the BIOMONITOR, in this patient population. By identifying AF, physicians can initiate appropriate

Fig. 1 Cumulative incidence of AF diagnosis by 12 months



management strategies, including anticoagulation therapy, to reduce the risk of recurrent stroke.

Acknowledgements The authors thank the CERTITUDE Steering Committee for their thoughtful review of this analysis.

Funding CERTITUDE program activities are supported financially by BIOTRONIK, Inc.

Data Availability Due to Data Use Agreement with CMS, supporting data is not available.

Declarations

Ethics approval This retrospective analysis was conducted utilizing real-world evidence methodology, which has been approved by an institutional review board. The research reported in this study adhered to the guidelines set forth by the Office of Human Research Protection that is supported by the US Department of Health and Human Services.

Competing interests Steven Mullane, Camden Harrell, and David Hayes are employed by BIOTRONIK, Inc. Niko Tsitiridis is employed by BIOTRONIK SE & Co. KG. Jim W. Cheung and Gaurav Upadhyay received consulting fees from BIOTRONIK, Inc. and serve on the steering committee of CERTITUDE.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Yaghi S, Bernstein RA, Passman R, Okin PM, Furie KL. Cryptogenic stroke: research and practice. *Circ Res.* 2017;120(3):527–40.
2. Sanna T, Diener HC, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, Rymer MM, Thijs V, Rogers T, Beckers F, Lindborg K, Brachmann J, CRYSTAL AF Investigators. Cryptogenic stroke and underlying atrial fibrillation. *N Engl J Med.* 2014;370(26):2478–86.
3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Dan G, Dilaveris PE, Fauchier L, Filippatos G, Kalman J, La Meir M. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2020;00:1–125.
4. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockcroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O, Meschia JF, Nguyen TN, Pollak PM, Santangeli P, Sharrief AZ, Smith SC Jr, Turan TN, Williams LS. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke.* 2021;52(7):e364–467.
5. National Institute for Health and Care Excellence (2020) Implantable cardiac monitors to detect atrial fibrillation after cryptogenic stroke. Diagnostics guidance [DG41]
6. Deshmukh AJ, Harrell C, Hicks J, Killu AM, Mulpuru SK, Asirvatham SJ, Friedman PA, Cha YM, Madhavan M. Physical activity in cardiac implantable electronic device recipients during the COVID-19 pandemic. *Mayo Clin Proc.* 2022;97(8):1493–500.
7. Chronic Conditions Data Warehouse (2017) 27 CCW Chronic Conditions (1999–2021). CMS Medicare and Medicaid research data. Accessed 5 May 2023. <https://www2.ccwdata.org/web/guest/condition-categories-chronic>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.