Device-Detected Atrial Fibrillation

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EDITORIAL

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Evidencing the Knowledge Gap

Article, see p 2502

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Stroke is a devastating complication of atrial fibrillation (AF), the odds of which can be reduced by use of oral anticoagulation based on the stroke risk score.[1,2] Patients with asymptomatic clinical AF have a similar stroke risk as patients with symptomatic clinical AF.[3] Thus far, electrocardiographic (ECG)- or Holter monitor–detected AF is a prerequisite before use of oral anticoagulation,[1,2] because the guideline recommendations are based on studies that included only ECG- or Holter-detected AF ("clinical" AF).[1,2] In recent decades, increasing number of cardiac implantable electronic devices (CIED) have been implanted in patients with cardiovascular diseases, predominantly driven by expanding indications for implantable cardioverter defibrillators, cardiac resynchronization therapy, and implantable loop recorders. These CIEDs can detect atrial high rate episodes, ie, atrial arrhythmias.[4–6] As a consequence of continuous monitoring by these devices, the detection threshold for atrial tachyarrhythmias or AF has decreased dramatically. However, AF detection algorithms, sensitivity, and specificity vary between CIEDs, and this may have an impact on the usage for AF detection purposes.[7]

Atrial tachyarrhythmias detected on atrial leads (ie, device-detected AF) occur frequently in patients with CIED and are associated with an increased risk of stroke.[8] However, when comparing stroke risks between device-detected (subclinical) and clinical AF for patients with identical stroke risk scores, stroke risk is lower in patients with device-detected AF.[6,9,10] Lowering the detection threshold by increasing the density of AF monitoring from sporadic capture with an ECG, to 24- or 48- or 72-hour continuous Holter monitoring, to continuous 24-hours-a-day, 7-days-a-week monitoring for years may identify patients with very rare episodes of AF who could have a different (and potentially lower) stroke risk than patients who present with clinical AF, as included in current stroke prevention trials.[7] Because of the paucity of data on this topic, both American and European guidelines on AF currently recommend confirming subclinical or device-detected AF with ECG or Holter monitoring before starting oral anticoagulation.[1,2]

In this issue of *Circulation*, Perino et al[11] describe variation in oral anticoagulation prescription between different practices in response to new device-detected AF. The findings were based on a retrospective cohort study using data from the Veterans Health Administration and included 10 212 patients with CIED with remote monitoring (Carelink; Medtronic) aiming to assess day-to-day AF burden. Variation in oral anticoagulation practice was also assessed across a range of AF duration thresholds (from ≥6 minutes to >24 hours). The authors report several interesting findings. First, device-detected AF occurred in nearly half of the patients (4570 of 10 212 [45%]). When considering only those with at least 1 hour of device-detected AF, 1712 of 10 112 (17%) had device-detected AF. After detection of device-

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detected AF, the percentage of patients in whom oral anticoagulation was started varied by AF duration, and increased from 13% in those with at least 1 episode of AF >6 minutes, to 16% in those with an AF episode >1 hour, to 21% in those with an episode >6 hours, and to 27% in those with an episode >24 hours. Second, they observed a wide variation between the 52 US sites in prescribing anticoagulation. In patients with a device-detected AF episode of >1 hour in one site, only 3% of patients were anticoagulated, whereas in another site, up to 67% of patients were anticoagulated. Similar variation (between 0% and 60%) was seen in patients with at least 1 device-detected AF episode >24 hours. Based on these data, there seems to be a large difference in how physicians interpret device-detected AF in CIED patients. Last, the authors found that particularly patients with at least 1 episode of device-detected AF >24 hours had the highest risk of stroke and that the risk was lowered in those who were treated with anticoagulation (hazard ratio: 0.28).

As with any observational study, there are several limitations, most of which are pointed out by the authors. An important source of bias that needs consideration is the inclusion of predominantly implantable cardioverter defibrillator patients. Many of these patients had heart failure and other stroke risk factors, and AF is known to be frequently present in this population. Also, the indications for implantable loop recorders were not reported; it is possible that in some patients the recorders were implanted because of suspicion of AF. Furthermore, there is limited information on associated cardiovascular conditions and diseases. Also, patients with clinical AF were excluded from the present analysis, though it is possible that some of these patients are actually patients with device-detected AF, followed by ECG or Holter AF confirmation. Furthermore, it is unknown to what extent the treating physician was aware of the arrhythmia detection by the device, and how and whether they assessed the risk of stroke as being too low to justify starting anticoagulation. It is important to note that the $CHADS_2$/CHA_2DS_2-VASc risk scores are validated in cohorts of patients with clinical AF, not subclinical or device-detected AF. Finally, adjudication of device-detected episodes was not performed, so misdiagnosis may well be possible. These selection biases, together with a high a priori chance of finding AF in implantable cardioverter defibrillator patients, may hamper generalizability of the findings.

Despite these limitations, the authors should be congratulated for their contribution to the literature. They confirm that device-detected AF is a rather common finding and that use of anticoagulation varies enormously among doctors. This again underscores (1) the importance of randomized trials in patients with device-detected AF, and (2) the fact that we may need to reconsider our thinking about temporality of AF and stroke. Currently, 2 large randomized trials are underway that may help to increase our understanding of both issues. The ARTESiA trial (Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Subclinical Atrial Fibrillation) aims to include 4000 patients, and in 2021 the results are expected (URL: https://www.clinicaltrials.gov; Unique Identifier: NCT01938248).[12] The NOAH study (Non–Vitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes) aims to include 2686 patients, and in 2022 their results are expected (URL: https://www.clinicaltrials.gov; Unique Identifier: NCT02618577).[13] Furthermore, the RACE V consortium (Reappraisal of Atrial Fibrillation: Interaction Between Hypercoagulability, Electrical Remodelling, and Vascular Destabilisation in the Progression of AF) aims to study the possible role of hypercoagulability as a potential final common pathway in the development of stroke and AF. Experimental data suggest that AF can cause and be the consequence of hypercoagulability. AF can cause a hypercoagulable state by initiating a profibrotic and proinflammatory response, and hypercoagulability seems to promote the development of AF substrate and AF progression to vascular risk via hypercoagulability.[14]

In conclusion, the paper by Perino et al provided evidence of an important knowledge gap, where additional research is eagerly needed in order to help clinicians make personalized treatment decisions for treatment with oral anticoagulation in patients with device-detected AF.

ARTICLE INFORMATION

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Disclosures

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REFERENCES

1. January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, Jr, Ellinor PT, Ezekowitz MD, Field ME, Furie KL, Heidenreich PA, Murray KT, Shea JB, Tracy CM, Yancy CW. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Circulation*. 2019; 139: 2502–2512. doi: 10.1161/CIRCULATIONAHA.118.038988
2. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Authors/Task Force Mem-

bers, Document Reviewers:. 2016 ESC Guidelines for the Management of Atrial Fibrillation Developed in Collaboration with EACTS: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESCEndorsed by the European Stroke Organisation (ESO). *Eur Heart J.* 2016; 38: 2893–2962.

3. Xiong Q, Proietti M, Senoo K, Lip GY. Asymptomatic versus symptomatic atrial fibrillation: a systematic review of age/gender differences and cardiovascular outcomes. *Int J Cardiol.* 2015;191:172–177. doi: 10.1016/j.ijcard.2015.05.011
4. Boriani G, Glotzer TV, Ziegler PD, De Melis M, Mangoni di S Stefano L, Sepsi M, Landolina M, Lunati M, Lewalter T, Camm AJ. Detection of new atrial fibrillation in patients with cardiac implanted electronic devices and factors associated with transition to higher device-detected atrial fibrillation burden. *Heart Rhythm.* 2018;15:376–383. doi: 10.1016/j.hrthm.2017.11.007
5. Glotzer TV, Daoud EG, Wyse DG, Singer DE, Ezekowitz MD, Hilker C, Miller C, Qi D, Ziegler PD. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnostics and stroke risk: the TRENDS study. *Circ Arrhythm Electrophysiol.* 2009;2:474–480. doi: 10.1161/CIRCEP.109.849638
6. Healey JS, Connolly SJ, Gold MR, Israel CW, Van Gelder IC, Capucci A, Lau CP, Fain E, Yang S, Bailleul C, Morillo CA, Carlson M, Themeles E, Kaufman ES, Hohnloser SH; ASSERT Investigators. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med.* 2012;366:120–129. doi: 10.1056/NEJMoa1105575
7. Kotecha D, Breithardt G, Camm AJ, Lip GYH, Schotten U, Ahlsson A, Arnar D, Atar D, Auricchio A, Bax J, Benussi S, Blomstrom-Lundqvist C, Borggrefe M, Boriani G, Brandes A, Calkins H, Casadei B, Castella M, Chua W, Crijns H, Dobrev D, Fabritz L, Feuring M, Freedman B, Gerth A, Goette A, Guasch E, Haase D, Hatem S, Haeusler KG, Heidbuchel H, Hendriks J, Hunter C, Kaab S, Kespohl S, Landmesser U, Lane DA, Lewalter T, Mont L, Nabauer M, Nielsen JC, Oeff M, Oldgren J, Oto A, Pison L, Potpara T, Ravens U, Richard-Lordereau I, Rienstra M, Savelieva I, Schnabel R, Sinner MF, Sommer P, Themistoclakis S, Van Gelder IC, Vardas PE, Verma A, Wakili R, Weber E, Werring D, Willems S, Ziegler A, Hindricks G, Kirchhof P. Integrating new approaches to atrial fibrillation management: the 6th AFNET/EHRA Consensus Conference. *Europace.* 2018;20:395–407.
8. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER III, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive Summary: Heart Disease and Stroke Statistics–2014 update: a report from the American Heart Association. *Circulation.* 2014;129:399–410. doi: 10.1161/01.cir.0000442015.53336.12
9. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA.* 2001;285: 2864–2870.
10. Chen-Scarabelli C, Scarabelli TM, Ellenbogen KA, Halperin JL. Device-detected atrial fibrillation: what to do with asymptomatic patients? *J Am Coll Cardiol.* 2015;65:281–294. doi: 10.1016/j.jacc.2014.10.045
11. Perino AC, Fan J, Askari M, Heidenreich PA, Keung E, Raitt MH, Piccini JP, Ziegler PD, Turakhia MP. Practice variation in anticoagulation prescription and outcomes after device-detected atrial fibrillation: insights from the Veterans Health Administration. *Circulation*. 2019;139:2502–2512. doi: 10.1161/CIRCULATIONAHA.118.038988
12. Lopes RD, Alings M, Connolly SJ, Beresh H, Granger CB, Mazuecos JB, Boriani G, Nielsen JC, Conen D, Hohnloser SH, Mairesse GH, Mabo P, Camm AJ, Healey JS. Rationale and design of the Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial. *Am Heart J.* 2017;189:137–145. doi: 10.1016/j.ahj.2017.04.008
13. Kirchhof P, Blank BF, Calvert M, Camm AJ, Chlouverakis G, Diener HC, Goette A, Huening A, Lip GYH, Simantirakis E, Vardas P. Probing oral anticoagulation in patients with atrial high rate episodes: rationale and design of the Non-vitamin K antagonist Oral anticoagulants in patients with Atrial High rate episodes (NOAH-AFNET 6) trial. *Am Heart J.* 2017;190:12–18. doi: 10.1016/j.ahj.2017.04.015
14. Spronk HM, De Jong AM, Verheule S, De Boer HC, Maass AH, Lau DH, Rienstra M, van Hunnik A, Kuiper M, Lumeij S, Zeemering S, Linz D, Kamphuisen PW, Ten Cate H, Crijns HJ, Van Gelder IC, van Zonneveld AJ, Schotten U. Hypercoagulability causes atrial fibrosis and promotes atrial fibrillation. *Eur Heart J.* 2017;38:38–50. doi: 10.1093/eurheartj/ehw119