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Cardiac implantable electronic device-detected atrial fibrillation—“To anticoagulate or not to anticoagulate, that is the question”: The noble or ignoble choice?

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Atrial fibrillation (AF) detected during interrogation of a cardiovascular implantable electronic device (CIED) is a common event,¹ with available studies suggesting that it is associated with an increased risk of stroke.^{2,3} While current guidelines recommend oral anticoagulant (OAC) therapy for patients with AF and an elevated CHA₂DS₂-VASc score,⁴ controversy exists about whether the various components of CIED-detected AF (eg, duration, burden, and CHA₂DS₂-VASc score) predict stroke and, if effective as predictors, which characteristics best define that risk.⁵ As a result of this uncertainty, physicians concerned about thromboembolic risk often recommend OAC therapy for patients with CIED-detected AF. This was demonstrated in Predicting Determinants of Atrial Fibrillation or Flutter for Therapy Elucidation in Patients at Risk for Thromboembolic Events (PREDATE AF) Study and REVEAL AF studies, in which, respectively, 76.4% and 56.3% of patients meeting predefined duration criteria for new-onset CIED-detected AF were prescribed anticoagulants.^{6,7}

In this issue of the Heart Rhythm Journal, Al-Gibbawi et al⁸ address this clinical topic by investigating the roles of AF threshold burden (1%, 1%–10%, and >10%), duration of the longest AF episode (≤6, 6–24, and >24 hours), and the CHA₂DS₂-VASc score (1, 2–5, and ≥6) in predicting a subsequent stroke or transient ischemic attack (TIA) over a mean of 3.26 ± 0.8 years in a retrospective record review of nonanticoagulated patients with CIED-detected AF at their institution. The incidence of new stroke or TIA at follow-up was 14.8%. After adjusting for the CHA₂DS₂-VASc score, neither the overall burden (P = .582) nor the longest single AF episode (P = .544) predicted stroke- or TIA-free survival. Importantly, after multivariate analysis, the CHA₂DS₂-VASc score remained an independent predictor of stroke- or TIA-free survival when analyzing models incorporating both the AF burden and the single longest AF episode duration (P = .001). Additionally, the stroke/TIA risk increased as the CHA₂DS₂-VASc score increased (P = .001). Therefore, this study provides evidence that intrinsic stroke risk factors, defined by the CHA₂DS₂-VASc score, serve as better and independent predictors of a subsequent stroke than do either AF duration or burden. While these findings are important, the older age (76.7 years vs 69.8 years; P = .0001) and the higher prevalence rates of peripheral arterial disease (38.6% vs 21.7%; P = .011), hypertension (91.2% vs 77.7%; P = .02), and hyperlipidemia (82.5% vs 59.6%; P = .01) in patients presenting with a stroke or TIA raise the possibility that alternative causative etiologies might have been operative in an unknown number of cases.

These findings are consistent with the results of the Registry of Atrial Tachyarrhythmia/Atrial Fibrillation (AT/AF) Episodes in the Cardiac Rhythm Management

(CRM) Device Population (RATE Registry), in which AF duration failed to predict subsequent stroke,⁹ and of the Mode Selection Trial (MOST),¹⁰ Danish Multicenter Randomized Trial on Single Lead Atrial Pacing versus Dual Chamber Pacing in Sick Sinus Syndrome (Danpace) Trial,¹¹ and West Birmingham Atrial Fibrillation Project¹² studies, in which the CHA2DS2-VASc score was an independent predictor of death or stroke in patients with a CIED irrespective of the AF history. The Italian AT500 Registry, in which the underlying CHADS2 score had a higher predictive value than did AF duration, adds further evidence to the primacy of the underlying risk factors.¹³ Data from The Relationship Between Daily Atrial Tachyarrhythmia Burden From Implantable Device Diagnostics and Stroke Risk: The TRENDS Study,

Asymptomatic Atrial Fibrillation and Stroke Evaluation in Pacemaker Patients and the Atrial Fibrillation Reduction Atrial Pacing Trial (ASSERT) & Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices (IMPACT) AF studies, in which a significant majority of patients did not have AF in the 30 days preceding a thromboembolic event, strengthen the argument that AF temporal characteristics have a lower predictive accuracy when compared to the risk factor profile.¹⁴⁻¹⁶ Importantly, the results provided in this and other published studies, which position the risk factor profile defined by the CHA2DS2-VASc score as the most powerful independent predictor of stroke in patients with CIED-detected AF, align with the atrial myopathy theory suggesting that AF may function more as a marker of stroke risk than as its cause. However, given the existing state of the art, more definitive recommendations about whether the temporal AF characteristics, the risk profile, or a combination should best guide anticoagulation strategies in patients with CIED-detected AF will need to await outcomes generated from ongoing trials including Apixaban for the Reduction of Thrombo- Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (Artesia Study: ClinicalTrials.gov identifier NCT01938248; accessed October 28, 2020), Nonvitamin K Antagonist Oral Anticoagulants in Patients With Atrial High Rate Episodes (NOAH-AFNET 6 Study: ClinicalTrials.gov identifier NCT02618577; accessed October 28, 2020), and the Atrial Fibrillation Detected by Continuous ECG Monitoring study (LOOP Study: ClinicalTrials.gov identifier NCT02036450; accessed October 28, 2020) designed to assess this question.

In the interim, while awaiting results from those investigations, physicians should base clinical decisions on approaches suggested in the 2017 European Heart Rhythm Association consensus document¹⁷ and the 2019 American College of Cardiology/American Heart Association/Heart Rhythm Society Focused AF Update.⁴ At present, it appears reasonable for physicians to pursue a binary approach when considering OAC choices among patients with CIED-detected AF. They should first try to identify low-risk patients (eg, low CHA2DS2-VASc score, low AF burden, and short AF duration) in whom OAC probably can be avoided. Efforts to identify higher-risk patients, in whom OAC might be advantageous, will remain speculative until results from these ongoing clinical trials become available. Until then clinical decisions about initiating OAC therapy in these patients might be better rendered by placing more emphasis on the thromboembolic risk profile, as defined by the CHA2DS2-VASc score, and less emphasis on the temporal AF aspects.

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