What We Don't Know Might Harm Our Patients: AF Detection Utilizing a Single Chamber ICD

Steven Zweibel[1]

[1]Hartford Hospital

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To the Editors of the Journal of Cardiovascular Electrophysiology:

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Thank you,

Steven Zweibel MD

Title: What We Don't Know Might Harm Our Patients: AF Detection Utilizing a Single Chamber ICD

Short Title: Atrial Arrhythmia Detection in Single Chamber ICD Patients

Steven L. Zweibel MD, FACC, FHRS

From Hartford HealthCare, Heart & Vascular Institute, Hartford, Connecticut

Address reprint requests and correspondence: Dr Steven Zweibel, Hartford HealthCare Heart & Vascular Institute, 65 Memorial Road, Suite 405, West Hartford CT 06107. E-mail address: steven.zweibel@hhchealth.org.

It is well known that patients receiving implantable cardioverter defibrillators are at risk for developing atrial fibrillation (AF) given their increased incidence of structural heart disease, heart failure, and other comorbidities.[1] Rates of new onset AF after ICD implant range from 10 to 45% over 6 months to 2.5 years after device implantation.[2-7] As AF may place patients at increased risk for inappropriate device therapy, some electrophysiologists consider implanting a dual chamber ICD in patients without a history of atrial arrhythmias despite the increased cost and risk of complications.[10] Beyond informing arrhythmia discriminators, the presence of an atrial lead provides valuable information by recording episodes of atrial arrhythmias which may otherwise be clinically silent. As device detected AF (DDAF) lasting between 5 minutes and 24 hours in patients with an annual rate of AF between 1.5% and 5% is associated with an increased risk of a thromboembolic event (HR ranging from 2.2 to 5.0)[2,3,6,8,9] data about clinically silent AF is vital. The lack of an atrial lead arguably puts clinicians at a disadvantage in assessing the presence of silent AF in patients with single chamber ICDs. As many of these patients have significant risk factors for stroke - including AF - what we don't know may harm our patients.

In this issue of the *Journal of Cardiovascular Electrophysiology* , Patel et. al. examines a new ventricular based AF detection algorithm present in single chamber ICDs (Medtronic Visia AF devices) to quantify the device-detected daily burden of AF and report on clinical actions taken after DDAF was recorded.[13] 291

patients were enrolled from Medtronic's Product Surveillance Registry over a period of about 4 years with a mean follow-up of 22.5 ± 7.9 months. 212 of these patients had no prior history of AF at the time of device implant. Since the device detects AF as an irregular ventricular response, atrial flutter and atrial tachycardia that conduct irregularly to the ventricles could also be detected. As the algorithm detects episodes lasting 6 minutes or longer, episodes with shorter duration may be undetected. Episodes of DDAF were adjudicated by an independent panel of electrophysiologists on the patient level – so if a patient had one episode that was deemed to be consistent with AF, all episodes that were recorded as AF were also deemed to be true DDAF. Of the 212 patients enrolled, 66% were male with a mean CHADS$_2$-VASc score of 3.3 ± 1.6 and a mean left ventricular ejection fraction of 33 ± 13%. The total incidence of any duration of AF ([?] 6 minutes) in patients without any prior history of AF was 38% with the median time to the first episode of DDAF being 104 days. At one year follow-up after device implantation, the Kaplan Meier rates of DDAF with daily burden [?] 6 minutes, > 6 hours, and >23 hours were 33%, 10%, and 3% respectively. At 2-year follow-up after device implantation, the rates of DDAF with daily burden [?] 6 minutes, > 6 hours, and >23 hours were 41%, 13%, and 7% respectively. After independent review of these DDAF episodes it was determined that true AF was documented in 100% of the >23 hours, 75% of the > 6 hours, and 40% of the [?] 6 minutes cohorts. So all recorded episode of AF lasting more than 23 hours were true AF. Of the 80 patients with DDAF episodes [?] 6 minutes, unfortunately only 23 patients were further evaluated for a clinical diagnosis, assessment of clinical symptoms, and to record actions taken in response to DDAF. The majority (17/23) of these patients were found to be asymptomatic, 9 patients were newly initiated on oral anticoagulation therapy (with all patients in the >23 hour burden category being anticoagulated), and 2 were initiated on antiarrhythmic drug therapy. The authors found that while clinical action was taken across the whole spectrum of CHADS$_2$-VASc scores, more clinical action was taken for those patients with higher AF burden. They conclude that continuous AF monitoring with this new ventricular based AF detection algorithm in the Visia AF ICDs permits early identification and actionable treatment for patients with undiagnosed AF.

This study demonstrates that patients receiving single chamber ICDs have a significant incidence of AF. The novel algorithm present in Visia AF is effective at detecting these episodes. However, significant questions remain. For example, does clinically-silent AF detected by a CIED carry the same risk of stroke as AF that is clinically manifest? And what percentage of AF burden recorded by a device should prompt the initiation of anticoagulation? Kaplan et. al. studied the risk of stroke and systemic embolism (SSE) as a function of AF duration and CHADS$_2$-VASc score in patients with cardiovascular implantable electronic devices (CIEDs) using medical record data from the Optum de-identified EHR linked to the Medtronic CareLink database.[14] They found that among 21,768 nonanticoagulated patients with CIEDs, both increasing AF duration and increasing CHADS$_2$-VASc score were significantly associated with annualized risk of SSE. SSE rates were low (<1% per year) in patients with CHADS$_2$-VASc scores of 0 to 1 regardless of the device-detected AF duration. However, stroke risk exceeded a rate of 1%/year in patients with a CHADS$_2$-VASc score of 2 and an AF duration >23.5 hours, those with a CHADS$_2$-VASc score of 3 to 4 and an AF duration >6 minutes, and in patients with a CHADS$_2$-VASc score of [?]5 even with no AF. This suggests a strong association between the CHADS$_2$-VASc score and the future risk of stroke with some role for the duration of AF detected by the CIED. Al-Gibbawi et. al. studied 384 patients with CIEDs with atrial leads who were not anticoagulated and noted that the incidence of stroke or TIA was 14.8% over 3.2 years but was not associated with the burden of AF or with the longest episode of AF but was strongly associated with the CHADS$_2$-VASc score.[15] This study suggests that once AF is detected on a device, regardless of duration, the decision to initiate anticoagulation on a patient should be based off of the CHADS$_2$-VASc score.

Fortunately, on-going trials are exploring the question of when patients with CIED detected AF should be anticoagulated. The Artesia Study (ClinicalTrials.gov Identifier NCT01938248) is examining the potential benefit of apixaban versus aspirin in patients with sub-clinical AF ([?] 175 bpm atrial rate and [?] 6 minutes duration) detected by their implantable cardiac device in the prevention of stroke and systemic embolism. The NOAH-AFNET 6 Study (ClinicalTrials.gov Identifier NCT02618577) is examining the potential benefit of edoxaban versus aspirin or a placebo in patients with atrial high-rate episodes ([?] 170 bpm atrial rate and [?] 6 minutes duration) detected by their implantable cardiac device in the prevention of stroke, systemic

embolism, and cardiovascular death. Until the results of these trials are published, it is reasonable to utilize the patient's risk profile for a thromboembolic event, as measured by their CHADS$_2$-VASc score, to assist in the decision-making process once AF is detected by their device. Having an algorithm in single chamber ICDs that can reliably detect AF and allow us to have these conversations with our patients to help make informed decisions is critically important. After all, what we don't know about our patients could indeed bring them harm.

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