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Pacemakers as Atrial Fibrillation Detectors: Finding Racial Differences and Opportunities for Preventing Stroke

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Implantation of permanent pacemakers has become routine and pervasive. Overall use increased by 53% between 1993 and 2009, with a significant steady decline in single-chamber ventricular devices throughout this time period and a significant steady rise in dual-chamber devices until around 2002, when the rates stabilized.[1] Beyond their self-evident therapeutic benefits, pacemakers can have important diagnostic utility. With atrial leads and current detection algorithms, these devices can detect atrial tachycardia with 95% accuracy.[2]

In this issue of *JAHA*, Kamel et al performed an observational study exploiting the fact that pacemakers can act as atrial fibrillation (AF) detectors; they analyzed administrative records from 2005–2006 to 2010–2011 from California, Florida, and New York of patients with permanent pacemakers and no history of AF.[3] After adjusting for demographic and clinical differences, investigators found a significantly lower risk of developing AF among black patients relative to white patients (hazard ratio 0.91). The study has several strengths, including its size, involving >100 000 participants. Furthermore, incident AF was assessed in a manner less prone to ascertainment bias than review of administrative records of a population lacking pacemakers. The study, however, relied on administrative records rather than direct interrogation of the pacemakers and may still have suffered from some level of ascertainment bias because transient runs of AF may not have been documented with the same rigor across racial groups. In addition, although the study adjusted for pacemaker interrogations, it did not adjust for type of device, atrial lead placement, or diagnostic algorithm, all of which may contribute to variations in sensitivity for detecting AF. The findings of Kamel et al were largely consistent with those of ASSERT, the Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial, which also found lower rates of AF in black participants relative to white participants.[4] Table compares key features of the 2 studies.

Differences in population genetics may explain the lower risk of AF among black participants relative to white participants. An approach to testing this hypothesis is through admixture mapping, which assumes that differences in rates of a phenotype are caused by differences in the frequency of phenotype-causing genetic variants between populations. After adjusting for numerous potential confounders including age, sex, body mass index, diabetes mellitus, and heart failure, a meta-analysis of Atherosclerosis Risk in Communities (ARIC), which included 4543 white and 822 black participants, and the Cardiovascular Health Study (CHS), which included 10 902 white and 3517 black participants, showed that for every 10% increase in European ancestry, there was a 13% increase in the risk of AF.[5] The findings in ARIC and in CHS were not statistically heterogeneous. In the case of ARIC, a significant relationship between European ancestry and risk of AF was independently observed using 2 separate arrays of ancestry-informative markers. Nevertheless, among postmenopausal women in the Women's Health Initiative (WHI), genomewide ancestry did not associate with AF, even though self-reported African American race/ethnicity was negatively associated with AF.[6] The reasons for failure to replicate are uncertain, but the degree of European ancestry in the WHI cohort was low, and classification of AF relied on self-report, potentially compromising power to detect differences.

Kamel et al evaluated patients for the presence or absence of AF; however, the arrhythmia is not a dichotomous trait.[3] The reality is more complex. Patients with AF are more appropriately seen as having varying degrees of disease burden. The risk of stroke is higher for patients with permanent versus nonpermanent AF, and, somewhat surprisingly, anticoagulation may not negate this difference. The AMADEUS study found that the risk of cardiovascular death, stroke, or systemic embolism is 68% higher in anticoagulated patients with permanent versus nonpermanent AF.[7] For every

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Table. Studies of Incident Atrial Fibrillation in Patients With Permanent Pacemaker Implantation Showing Higher Rates Among White Than Black Participants

Study	Population	Sample (n)	Definition of Incident AF	Length of Follow-up (Years)	Incidence Rates (%)	
					White	Black
Lau et al, 2013[4]	Patients from 23 countries in North America, Europe, and Asia in ASSERT trial	2559	AF episode >190/min lasting >6 min	2.5	18	8.3
Kamel et al, 2016[3]	Patients from California, Florida, and New York hospitalized or seen in an Emergency Department	101 773	ICD-9-CM codes for AF	3.7±1.8	21.4	25.5

AF indicates atrial fibrillation; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification.

hour increase in daily maximum of AF burden, the relative risk of stroke increases by ≈3%.[8]

Although rarely immediately life threatening, AF cannot be ignored. AF is one of the most important modifiable risk factors for ischemic stroke. Antithrombotic therapy dramatically reduces the risk of ischemic stroke in patients with AF. Patients with nonrheumatic AF treated with warfarin have an odds ratio of 0.58 of having stroke relative to patients treated with aspirin.[9] Recently, the therapeutic arsenal has expanded to include direct thrombin inhibitors and inhibitors of activated factor X, which are at least as safe and effective as warfarin for preventing stroke in patients with nonvalvular AF.[10]

There is reason to suspect considerable missed opportunities for preventing stroke related to nonpermanent AF. It is estimated that in the United States, there are 460 000 cases of undiagnosed AF in people aged ≥65 years and an additional 136 000 cases of undiagnosed AF in people aged 18 to 64 years.[11] Pacemaker detection of AF could reduce the burden of undiagnosed AF. Remote monitoring may help with earlier detection of clinically significant AF.[12]

Rates of pacemaker-detected AF may vary by race because rates of pacemaker placement may vary. Data from the National Hospital Discharge Survey (1996–2001) found that black patients were significantly less likely to be discharged with a permanent pacemaker for complete heart block than white patients (68% versus 80%).[13] Although one can reasonably hope that fewer disparities exist now than existed >14 years ago, more recent data from Pennsylvania regarding hospitalized patients with heart failure and left ventricular systolic dysfunction found that black patients are significantly less likely to get biventricular pacing (odds ratio 0.56).[14]

Racial disparities notwithstanding, there may be general undertreatment of pacemaker-detected AF. In a single academic hospital in Ontario, Canada, pacemaker-detected AF occurred in 50% of pacemaker patients and was treated in <25% of patients who did not have a history of clinical AF.[15]

When patients with pacemakers present with acute stroke and no history of AF, the pacemaker should be interrogated. This should be part of a workup that includes imaging of the carotid arteries to exclude symptomatic carotid stenosis. Diagnostic yield of interrogating permanent pacemaker memories is high in patients after cryptogenic stroke.[16] Without detection of some burden of AF, there is often no clear indication to treat with anticoagulants.

Pacemakers are clarifying the relationship between AF burden and risk of ischemic stroke. Pacemakers are also providing evidence of racial differences in risk of AF. Genomic studies suggest that background genetics may explain the observed racial risk difference, although as yet unknown differences in environmental exposures may also explain some of the racial disparity. There may be important disparities in pacemaker placement, and that aspect deserves more investigation. Once placed, however, a pacemaker should be seen as a tool for early detection of AF and used to reduce stroke risk through early anticoagulation.

Disclosures

None.

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