

TOPIC COLLECTION: DIAGNOSING, UNDERSTANDING, AND SCREENING FOR ATRIAL FIBRILLATION

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Letter from the Editor

A lot of recent attention has focused on approaches to detecting atrial fibrillation. In the NEJM article *Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation*, Perez and colleagues evaluated heart rate patterns in hundreds of thousands of people wearing the Series 3 Apple smartwatch. The actual findings suggested a need to improve the algorithm, but the study heralds a new era in which consumer products are getting ahead of medical knowledge by producing information whose value has not yet been defined. We do not yet know whether treatment for very brief episodes of atrial fibrillation has a net benefit. We have never had the capability to monitor millions of people in this way. Meanwhile, even as people are now being screened with these consumer products, the USPSTF is telling doctors that they do not need to routinely screen patients for atrial fibrillation with an electrocardiogram, and that pulse palpation is sufficient. However, with new smart watches, people are now commonly obtaining single lead rhythm strips. Many doctors are receiving calls and even emails about these tracings. So, we now have a hypervigilant population of people who are keyed into their heart rhythm, but the evidence needs to catch up. And for balance, not everyone is knowledgeable about atrial fibrillation. Even among people with documented atrial fibrillation, one study found that 1 in 5 did not know the condition was associated with a risk for stroke. There is still a need for basic education for many patients.

The NEJM Journal Watch summaries address these issues: Attia and colleagues see a positive role for artificial intelligence, while the study by Hijazi et al. addresses the need for patient education regarding risks associated with their condition. Finally, the USPSTF guidelines recommend pulse palpitation as sufficient screening in a general population of older adults.

Harlan M. Krumholz, MD, SM

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ORIGINAL ARTICLE

Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation

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ABSTRACT

BACKGROUND

Optical sensors on wearable devices can detect irregular pulses. The ability of a smartwatch application (app) to identify atrial fibrillation during typical use is unknown.

METHODS

Participants without atrial fibrillation (as reported by the participants themselves) used a smartphone (Apple iPhone) app to consent to monitoring. If a smartwatch-based irregular pulse notification algorithm identified possible atrial fibrillation, a telemedicine visit was initiated and an electrocardiography (ECG) patch was mailed to the participant, to be worn for up to 7 days. Surveys were administered 90 days after notification of the irregular pulse and at the end of the study. The main objectives were to estimate the proportion of notified participants with atrial fibrillation shown on an ECG patch and the positive predictive value of irregular pulse intervals with a targeted confidence interval width of 0.10.

RESULTS

We recruited 419,297 participants over 8 months. Over a median of 117 days of monitoring, 2161 participants (0.52%) received notifications of irregular pulse. Among the 450 participants who returned ECG patches containing data that could be analyzed — which had been applied, on average, 13 days after notification — atrial fibrillation was present in 34% (97.5% confidence interval [CI], 29 to 39) overall and in 35% (97.5% CI, 27 to 43) of participants 65 years of age or older. Among participants who were notified of an irregular pulse, the positive predictive value was 0.84 (95% CI, 0.76 to 0.92) for observing atrial fibrillation on the ECG simultaneously with a subsequent irregular pulse notification and 0.71 (97.5% CI, 0.69 to 0.74) for observing atrial fibrillation on the ECG simultaneously with a subsequent irregular tachogram. Of 1376 notified participants who returned a 90-day survey, 57% contacted health care providers outside the study. There were no reports of serious app-related adverse events.

CONCLUSIONS

The probability of receiving an irregular pulse notification was low. Among participants who received notification of an irregular pulse, 34% had atrial fibrillation on subsequent ECG patch readings and 84% of notifications were concordant with atrial fibrillation. This siteless (no on-site visits were required for the participants), pragmatic study design provides a foundation for large-scale pragmatic studies in which outcomes or adherence can be reliably assessed with user-owned devices. (Funded by Apple; Apple Heart Study ClinicalTrials.gov number, NCT03335800.)

From the Division of Cardiovascular Medicine (M.V.P.), Stanford Center for Clinical Research (K.W.M., A.R., N.T.), the Quantitative Sciences Unit (H.H., A.G., V.B., J.L., S.E.G., M.D.), Information Resources and Technology (T.F., G.H.), Department of Medicine (S.D.), and the Center for Digital Health (M.P.T.), Stanford University, Stanford, Apple, Cupertino (L.C., D.N., A.B., S.D.), and the Veterans Affairs Palo Alto Health Care System, Palo Alto (M.P.T.) — all in California; the University of Colorado School of Medicine, Aurora (J.S.R.); the Division of Cardiovascular Disease, Cooper Medical School of Rowan University, Camden, NJ (A.M.R.); the Lankenau Heart Institute and Jefferson Medical College, Philadelphia (P.K.); StopAfib.org, American Foundation for Women's Health, Decatur, TX (M.T.H.); and the Duke Clinical Research Institute, Duke University, Durham, NC (C.B.G.). Address reprint requests to Dr. Perez or Dr. Turakhia at Stanford Center for Clinical Research, 1070 Arastradero Rd., Palo Alto, CA 94304, or at mvperez@stanford.edu or mintu@stanford.edu.

*A complete list of the Apple Heart Study Investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Using Artificial Intelligence to Predict Atrial Fibrillation

An algorithm using machine learning to analyze ECGs in patients in normal sinus rhythm may eventually improve care of an at-risk population.

The diagnosis of atrial fibrillation (AF) requires an electrocardiogram (ECG) during an AF episode although structural atrial changes and grossly abnormal ECG findings such as left atrial enlargement can also point to AF. However, if ECGs in normal sinus rhythm provided clues to the risk for AF, then more individuals could be evaluated closely for AF before the clinical diagnosis and receive treatment. These researchers hypothesized that more subtle ECG findings during normal sinus rhythm are also associated with AF.

In a retrospective ECG database of 180,922 patients with 649,931 ECGs, machine learning through artificial intelligence (AI) was used to develop a predictive model for AF from a single, normal sinus rhythm ECG. Approximately two thirds of ECGs were used for the training set, and the remainder were used for validation and testing. About 8% of patients in the testing cohort had verified AF diagnoses, based on earlier ECGs.

The AI algorithm performed quite well. The area under the curve of the receiver operating characteristic curve for detecting AF was 0.87 in the derivation and validation sets. When applied to the testing group, the sensitivity was 79.0%, the specificity was 79.5%, and the overall accuracy was 79.4%.

COMMENT

AF can be intermittent for many years and is often not diagnosed until patients have progressed to longer episodes. Diagnosing AF earlier would allow treatment that could reduce the risk for cryptogenic stroke. The AI algorithm developed here is reasonably accurate. Certainly, at this time, treatment decisions should not be based on the algorithm, but it would enable more intense ECG monitoring for people predicted to be at heightened AF risk. — **Mark S. Link, MD**

Dr. Link is Professor of Medicine, Director, Cardiac Electrophysiology, UT Southwestern Medical Center, Dallas; and Deputy Editor, *NEJM Journal Watch Cardiology*

Attia ZI et al. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: A retrospective analysis of outcome prediction. Lancet 2019 Aug 1; [e-pub]. (https://doi.org/10.1016/S0140-6736(19)31721-0)

Patients with Atrial Fibrillation Might Not Be Accurately Perceiving Their Risks

Many patients are making decisions with mistaken impressions of their risks.

For patients with atrial fibrillation (AF), decisions about oral anticoagulation to reduce the risk for stroke can be challenging and depend on their accurate assumptions about the risks and benefits of this strategy. To determine patients' knowledge, investigators associated with the largest West Virginia teaching hospital invited consecutive patients with AF presenting to an outpatient clinic or admitted to a low-acuity, non-critical care inpatient service to participate in an interview.

Of 287 interviewed patients, 21% were unaware that AF was associated with an increased stroke risk and were excluded from further questions. The 227 remaining patients (mean age, 72; 55% men; high school education or less, 70%) had a mean CHA₂DS₂-VASC score of 4.3 and a mean HAS-BLED score of 2.3. Almost 50% had been diagnosed with AF >5 years previously, and 60% were taking oral anticoagulation.

Estimated and patients' perceived risks for either stroke or bleeding showed practically no correlation. About 53% of participants thought that their yearly risk for stroke exceeded 20%, including 20% who thought it exceeded 50% (yet only 9% had an estimated risk >10%). About 53% thought the annual risk for bleeding with anticoagulation was >10% (yet only 14% had an estimated risk ≥7%). About one in five participants thought that anticoagulation lowered stroke risk by 90% (when in fact trials have shown a risk reduction of roughly two thirds).

COMMENT

In this single-site, cross-sectional study, patients with AF often had inaccurate estimates for stroke risk, risk reduction with oral anticoagulation, and risk for bleeding with oral anticoagulation. Moreover, many patients did not even know that AF was associated with stroke risk. Although the study is relatively small, it signals what is likely true in many settings and demonstrates a need for more effective ways to ensure that patients are making informed choices.

— **Harlan M. Krumholz, MD, SM**

Hijazi M et al. Perception of the risk of stroke and the risks and benefits of oral anticoagulation for stroke prevention in patients with atrial fibrillation: A cross-sectional study. Mayo Clin Proc 2019 Jun; 94:1015. (https://doi.org/10.1016/j.mayocp.2018.08.043)

USPSTF Does Not Recommend Routine ECG Screening for Diagnosis of AF

Evidence is insufficient for assessing the value of electrocardiographic screening of asymptomatic adults for atrial fibrillation.

Sponsoring Organization: U.S. Preventive Services Task Force (USPSTF)

Background and Objective

According to a growing body of evidence, the frequency of electrocardiographic (ECG) screening is linearly correlated with the diagnosis of atrial fibrillation (AF), which typically leads to anticoagulation to prevent stroke. However, the threshold density of AF at which the risk for stroke becomes elevated remains unknown. Patients without increased risk for embolic events would face adverse effects from anticoagulation but no benefit. The USPSTF has now published recommendations on ECG screening for AF in older adults along with a separate, exhaustive literature review — 17 studies on 135,000 individuals aged >65 — on the benefits and harms of ECG screening and anticoagulation.

Key Points

- The USPSTF finds insufficient data to recommend ECG screening for AF in a general population of older adults.

- Although systematic ECG screening discovers more individuals with AF than does no screening, its diagnostic rate is not different from the rate with pulse palpation.
- Data on harms of ECG screening were not found.
- The USPSTF also reports guidelines from major organizations. In primary care settings, the American Heart Association/American College of Cardiology recommend pulse assessment followed by ECG if the pulse is irregular. The European Society of Cardiology is more aggressive, recommending pulse palpation or an ECG strip in people aged >65 and consideration of systematic ECG screening in those aged >75.

COMMENT

ECG screening for diagnosis of AF ranges from 6-second ECGs at a provider's office to intermittent ECGs, implantable monitors, and permanent pacemakers and implantable cardioverter-defibrillators that monitor continuously.

Interest in this topic is enormous. While the USPTF is appropriately conservative in its recommendations, I as a physician would be concerned if my patient was having long AF episodes (certainly,

lasting >24 hours, but even shorter, more frequent episodes). Despite the influential and fundamental principle of "do no harm," a more important principle is the Golden Rule — do unto others as you would have others do unto you. I would want to know that I had asymptomatic AF and would indeed want to be anticoagulated if those AF episodes were >24 hours and my CHA₂DS₂-VASc score was ≥1. Editorialists note that stroke is often not temporally related to AF, that the CHA₂DS₂-VASc score has shortcomings, and that we need to improve our understanding of atrial myopathy, which increases the risk for embolic events. — **Mark S. Link, MD**

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Goldberger JJ and Mitrani RD. Electrocardiographic monitoring for prevention of atrial fibrillation-associated cardioembolic stroke. *JAMA* 2018 Aug 7; 320:447. (<https://doi.org/10.1001/jama.2018.9185>)