Artificial Intelligence—Enabled Electrocardiogram for Atrial Fibrillation Identifies Cognitive Decline Risk and Cerebral Infarcts

Erika L. Weil, MD; Peter A. Noseworthy, MD; Camden L. Lopez, MS; Alejandro A. Rabinstein, MD; Paul A. Friedman, MD; Zachi I. Attia, PhD; Xiaoxi Yao, PhD, MPH; Konstantinos C. Siontis, MD; Walter K. Kremers, PhD; Georgios Christopoulos, MD; Michelle M. Mielke, PhD; Prashanthi Vemuri, PhD; Clifford R. Jack Jr, MD; Bernard J. Gersh, MB, ChB, DPhil; Mary M. Machulda, PhD, LP; David S. Knopman, MD; Ronald C. Petersen, MD, PhD; and Jonathan Graff-Radford, MD

Abstract

Objective: To investigate whether artificial intelligence—enabled electrocardiogram (AI-ECG) assessment of atrial fibrillation (AF) risk predicts cognitive decline and cerebral infarcts.

Patients and Methods: This population-based study included sinus-rhythm ECG participants seen from November 29, 2004 through July 13, 2020, and a subset with brain magnetic resonance imaging (MRI) (October 10, 2011, through November 2, 2017). The AI-ECG score of AF risk calculated for participants was 0-1. To determine the AI-ECG-AF relationship with baseline cognitive dysfunction, we compared linear mixed-effects models with global and domain-specific cognitive z-scores from longitudinal neuropsychological assessments. The AI-ECG-AF score was logit transformed and modeled with cubic splines. For the brain-MRI subset, logistic regression evaluated correlation of the AI-ECG-AF score and the high-threshold, dichotomized AI-ECG-AF score with infarcts.

Results: Participants (N=3729; median age, 74.1 years) underwent cognitive analysis. Adjusting for age, sex, education, and APOE ε4-carrier status, the AI-ECG-AF score correlated with lower baseline and faster decline in global-cognitive z-scores (P=.009 and P=.01, respectively, non-linear-based spline-models tests) and attention z-scores (P<.001 and P=.01, respectively). Sinus-rhythm-ECG participants (n=1373) underwent MRI. As a continuous measure, the AI-ECG-AF score correlated with infarcts but not after age and sex adjustment (P=.52). For dichotomized analysis, an AI-ECG-AF score greater than 0.5 correlated with infarcts (OR, 4.61; 95% CI, 2.45-8.55; P<.001); even after age and sex adjustment (OR, 2.09; 95% CI, 1.06-4.07; P=.03).

Conclusion: The AI-ECG-AF score correlated with worse baseline cognition and gradual global cognition and attention decline. High AF probability by AI-ECG-AF score correlated with MRI cerebral infarcts. However, most infarcts observed in our cohort were subcortical, suggesting that AI-ECG not only predicts AF but also detects other non-AF cardiac disease markers and correlates with small vessel cerebrovascular disease and cognitive decline.

© 2022 Mayo Foundation for Medical Education and Research

Artificial Intelligence—Enabled Electrocardiogram for Atrial Fibrillation

Atrial fibrillation (AF) is the most common cardiac rhythm abnormality and is implicated in up to one-third of ischemic strokes. Yet, AF is underdiagnosed, particularly when asymptomatic or paroxysmal. Up to one-third of patients with AF are asymptomatic; the risk of cerebrovascular events in these
patients appears to be higher than symptomatic AF after adjustment for CHA2DS2-VASc score (congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, stroke, or transient ischemic attack, vascular disease). Atrial fibrillation is also associated with cognitive decline and dementia, even after accounting for clinical strokes.

An artificial intelligence—enabled electrocardiography (AI-ECG) acquired during normal sinus rhythm was recently shown to identify the presence of paroxysmal AF. The ability of this AI-ECG algorithm to predict future AF up to 10 years before clinical diagnosis was later confirmed in a population-based study. Whether the AI-ECG for AF detection is associated with an increased risk of infarcts and cognitive decline is unknown.

Because the majority of infarcts in population-based studies are “silent” and AF has been associated with silent infarction and cognitive decline, we hypothesized that high AI-ECG-AF scores, potentially reflecting undiagnosed paroxysmal AF, were associated with greater risk of cerebral infarcts and cognitive decline. The objective of the current study was to determine if the AI-ECG algorithm for AF detection correlated with baseline cognitive dysfunction and subsequent cognitive decline as well as the presence of cerebral infarcts in participants of a population-based study.

METHODS
Participant Population
Participants enrolled in the longitudinal, population-based Mayo Clinic Study of Aging (MCSA) between ages 30 and 95 years were considered for inclusion in the present study. The full details of the MCSA design have been published previously. In brief, residents of Olmsted County, Minnesota, aged 70 to 89 years, were enumerated using the Rochester Epidemiology Project medical records linkage system in 2004. Those eligible were randomly selected and invited to participate in the MCSA. The sample was later expanded in 2012 to include individuals age 50 years and older and, in 2015, to include those age 30 years and older. Participants in the MCSA underwent serial neurologic and neuropsychological examinations at study visits, approximately 15 months apart. Those without contraindications were also invited to undergo brain magnetic resonance imaging (MRI).

Risk-Factor Assessment
The Rochester Epidemiology Project medical records linkage system was used for medical record abstraction of data including medical comorbidities, smoking status, and antiplatelet or anticoagulant usage. Atrial flutter was categorized as AF.

AI-ECG-AF Score
The AI-ECG-AF probability score (a measure of AF risk) was computed using an AI-ECG algorithm trained to analyze raw 12-lead ECG data to detect the “signature” of AF on the sinus-rhythm ECG. The algorithm was applied only to ECGs that showed normal sinus rhythm and not AF, but no other exclusions were applied. The full details of this AI algorithm have been previously published.

AI-ECG-AF Score and Cognition
Participant Selection. Participants from the MCSA who had been seen between November 29, 2004, and July 13, 2020, with one or more ECG showing sinus rhythm before baseline visit and one or more MCSA visit with complete cognition z-score data were included regardless of whether the participants underwent an MRI scan. Those with known history of AF or younger than the age of 50 years at baseline visit were excluded from the cognitive analysis.

AI-ECG-AF Score. The most recent ECG showing normal sinus rhythm obtained before the baseline MCSA visit was selected for AI-ECG analysis. The selected ECGs were obtained a median of 2 (range, 0 to 27) years before the baseline MCSA visit.

Cognitive Assessment. Details regarding specific neuropsychological assessments
performed at MCSA visits have been previously published. Follow-up visits occur approximately 15 months apart. Cognitive scores were calculated for each participant in each cognitive domain (attention, memory, language, and visuospatial). A global cognitive score was also generated based upon averaged z-scores across all domains.

### AI-ECG-AF Score and Presence of Infarcts

#### Participant Selection.

For the analysis of AI-ECG-AF score and presence of infarcts, we included MCSA participants who were 30 to 95 years of age with one or more ECG showing sinus rhythm who also underwent T2 fluid attenuation inversion recovery (FLAIR) MRI between October 10, 2011, and November 2, 2017. The earliest MRI was used when the participant had multiple MRIs. Participants without ECG or with unknown AF history were excluded. Participants with known history of AF were not excluded from the analysis of infarcts.

#### AI-ECG-AF Probability Score.

The most recent ECG showing normal sinus rhythm obtained before the participant’s MRI was selected for AI-ECG analysis. The selected ECGs were obtained a median of 3 (range, 0 to 26) years before MRI acquisition.

### MRI Evaluations of Infarcts.

Infarcts were evaluated on 3T two-dimensional (2D) FLAIR MRI co-registered to a magnetization-prepared rapid gradient-echo (MPRAGE) T1 MRI. The full details of infarct grading have been previously published. Briefly, cortical infarctions were defined as T2 FLAIR hyperintense lesions involving the cortex with a corresponding area of T1 hypointensity. Subcortical infarctions were defined as T2 FLAIR hyperintense lesions located in the white matter, infratentorial, and deep structures with hypointense center measuring 3 mm or greater in diameter on either T2 FLAIR or T1 sequences. All potential infarcts were initially identified by trained image analysts and afterward confirmed by a vascular neurologist (J.G.R.) to whom all clinical information was blinded. The intra-rater reliability was excellent (κ statistic, 0.92).

### Statistical Analysis

#### AI-ECG-AF Score and Cognition.

Descriptive statistics were used to summarize participant demographic data. To evaluate the relationship between baseline AI-ECG-AF score and change in cognition, three linear mixed-effects models were fit for cognitive z-scores in global cognition and in each cognitive domain (attention, memory, language, and visuospatial). Each model included random participant-specific effects on the intercept and the slope (change in z-score over time since baseline), which were potentially correlated. The models all had fixed-effect terms for age, sex, education, APOE ε4 status, and the interaction of each of the four preceding variables with time. All cognitive models were also adjusted for prior exposure to cognitive testing. (There was a covariate for whether a measurement was post-baseline [subject had been tested previously] versus baseline [no previous test].) For each cognitive z-score, the first model did not include AI-ECG-AF score, the second had an effect of AI-ECG-AF score on the baseline z-score only, and the third model had effects of AI-ECG-AF score on both the baseline z-score and the slope over time for longitudinal cognitive assessment. The association of AI-ECG-AF score with baseline z-score was tested by comparing the first two

### Table 1. Baseline Characteristics of Mayo Clinic Study of Aging Participants Included in the Analysis of the Association of AI-ECG-AF Score With Cognition

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N=3729</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>74.1 (67.4 to 80.6)</td>
</tr>
<tr>
<td>Male</td>
<td>1833 (49.2)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>1280 (34.3)</td>
</tr>
<tr>
<td>Some college</td>
<td>1699 (45.6)</td>
</tr>
<tr>
<td>College graduate</td>
<td>750 (20.1)</td>
</tr>
<tr>
<td>APOE ε4 carrier</td>
<td>1007 (27.0)</td>
</tr>
<tr>
<td>AI-ECG AF score</td>
<td>0.017 (0.004 to 0.071)</td>
</tr>
</tbody>
</table>

*AI-ECG-AF = artificial intelligence–enabled electrocardiogram–atrial fibrillation.

**Values are median (IQR) or n (%).”

https://doi.org/10.1016/j.mayocp.2022.01.026
www.mayoclinicproceedings.org

873
models; the association of AI-ECG-AF score with change in z-score over time was tested by comparing the second and third models. In both cases, a likelihood-ratio test was used to calculate a $P$ value for the test of association. The AI-ECG-AF score was logit transformed and modeled as a continuous variable using cubic splines to allow for a nonlinear relationship. The association between AI-ECG-AF score and the probability of an infarct showing on MRI was presented by plotting estimated infarct probability as a function of AF score. All $P$ values were calculated using likelihood ratio tests. A $P$ value of less than .05 was considered statistically significant.

An analysis was also performed with dichotomous AI-ECG-AF score to examine whether a high-threshold AI-ECG-AF score was associated with infarcts. In a prior study, an AI-ECG-AF score of greater than 0.5 was associated with a cumulative incidence of AF of 21.5% at 2 years and 52.2% at 10 years; therefore, a threshold of 0.50 was used in the present study. To determine whether the relationship between infarct risk and AI-ECG-AF score differs by sex, a model with age, sex, AI-ECG, and sex×AI-ECG interaction was compared with a model without sex × AI-ECG interaction. A subanalysis was then performed excluding patients with history of AF.

**FIGURE 1.** Estimated mean baseline global cognitive z-score (A) or change in slope of global cognitive z-score over time (B) vs baseline artificial intelligence—enabled electrocardiogram—atrial fibrillation (AI-ECG-AF) score is shown with 95% confidence bands by sex (top, female; bottom, male) and by APOE e4 carrier status. Higher AI-ECG-AF probability scores are associated with lower baseline global cognitive z-scores (A) and more rapid decline in global cognitive z-scores (B) in both sexes and regardless of APOE e4 carrier status.
Protocol Approvals Standard, Registrations, and Patient Consents
The study was approved by Mayo Clinic and Olmsted Medical Center Institutional Review Boards. Written informed consent was obtained from all MCSA participants.

Data Availability
De-identified data from the Rochester Epidemiology Project are available upon written request.

RESULTS
AI-ECG-AF Score and Cognition
A total of 3729 MCSA participants without history of AF had at least one visit with complete cognition scores and had an ECG showing sinus rhythm (used to determine AI-ECG-AF score). Participant characteristics are summarized in Table 1. The median age of all participants at baseline visit was 74.1 (IQR, 67.4 to 80.6) years and 49.2% (n=1833) were male. A total of 1007 individuals (27.0%) were APOE ε4 carriers. The median AI-ECG score was 0.017 (IQR, 0.004 to 0.071). There was a median of 2.2 (range, 0 to 27) years from time of ECG to first MCSA visit.

The baseline AI-ECG-AF score was associated with lower baseline and greater decline in global cognitive z-score (P=.009 and P=.01, respectively). This is shown in Figure 1, which depicts mean baseline cognitive z-score (Figure 1A) or mean slope of z-score over time (Figure 1B) vs AI-ECG-AF score, by sex and APOE ε4-carrier status, with 95% confidence bands. There was also an association between AI-ECG-AF score and lower baseline and longitudinal change in attention z-score (P<.001 and P=.01, respectively) (Figure 2). Lower baseline visuospatial z-score was associated with higher AI-ECG-AF scores (P<.001), but change over time in visuospatial z-score was not (P=.29). Neither memory (P=.42 and P=.22, respectively) nor language z-scores (P=.23 and P=.15, respectively) were associated with AI-ECG-AF scores at baseline or over time. The models were re-run with adjustment for number of neuropsychological test exposures, but the results did not significantly change.
AI-ECG-AF Score and Presence of Infarcts

A total of 1373 individuals in the MCSA underwent MRI and had ECG showing normal sinus rhythm (used to determine AI-ECG-AF score). The median age of MCSA participants at time of baseline MRI was 69.4 (IQR, 62.1 to 79.1) years and 53.0% (n=728) were male. Demographic information is summarized in Table 2. There were 136 participants (9.9%) with history of paroxysmal AF. Only 3.4% (n=47) of participants were anticoagulated, and 642 (46.8%) were on antiplatelet monotherapy; 26 (1.9%) were on combined antiplatelet and anticoagulation. At least one ischemic infarct (either cortical or subcortical) was identified in 214 (15.6%) patients. The majority (n=173) were subcortical infarcts; 72 infarcts were cortical. The median AI-ECG-AF score was 0.012 (IQR, 0.003 to 0.053). As a continuous measure, the AI-ECG-AF score was associated with the presence of infarcts (P<.001), but not after adjusting for age and sex (P=.52).

Of the 1373 individuals with an ECG showing sinus rhythm who underwent MRI, only 43 participants (3.1%) had an AI-ECG-AF score greater than 0.50 and were included for the dichotomized analysis of AI-ECG score and infarcts. Of those with AF score greater than 0.50, 24 (55.8%) had known history of AF. Without adjustment, this higher threshold of AI-ECG-AF score was strongly associated with infarcts (OR, 4.61; 95% CI, 2.45 to 8.55; P<.001) (Figure 3). After adjusting for age and sex, an AI-ECG-AF score greater than 0.50 remained associated with the presence of infarcts on MRI (OR, 2.09; 95% CI, 1.06 to 4.07; P=.03). There was no difference observed between males and females in the association of infarct risk with AI-ECG-AF score (P=.93 for a test of interaction). When participants with known history of AF (n=136) were excluded, an AI-ECG-AF score greater than 0.50 was not associated with infarct risk both without adjustment (OR, 2.33; 95% CI, 0.74 to 6.18; P=.14) and after adjusting for age and sex (OR, 0.99; 95% CI, 0.30 to 2.78; P=.99).

DISCUSSION

This study examined an AI-ECG algorithm previously shown to identify AF to determine whether AI-ECG-AF scores could predict the presence of cognitive changes or cerebral infarcts in participants from a longitudinal population-based study with cognitive testing and neuroimaging. The main finding is that the AI-ECG-AF score was associated with both baseline and future decline in global cognition and attention in individuals without known AF. In participants with ECG showing sinus rhythm, there was also an association between a high AI-ECG-AF score and presence of cerebral infarctions on MRI.

In population-based studies, infarcts, including silent infarcts, are associated with future cognitive decline and dementia. Silent cerebral infarcts can be detected on MRI in up to 40% of patients with AF and have also been associated with increased risk of future symptomatic stroke. Even in the absence of prior stroke, AF is associated with an increased risk of future cognitive impairment or dementia. The
Rotterdam study was one of the first to describe this relationship,\(^2^1\) and several subsequent studies have validated this association.\(^1^8,2^2-2^4\) The risk of future dementia appears to be strongest in younger patients with AF and increases with longer duration of exposure to this arrhythmia.\(^2^4\)

The pathophysiology behind the association of AF and cognitive dysfunction is not well understood but may be due to a combination of factors. Higher AI-ECG-AF probability scores, which predict future development of AF,\(^9\) were predictive of future global cognitive and attention decline in the current analysis. The AI-ECG score—associated cognitive decline appeared progressive, suggesting that AF-associated cognitive decline may not be entirely explained by cerebral infarctions visible on MRI alone, given that ischemic infarcts are expected to cause a more acute cognitive decline. Previous studies have reported reduced gray-matter volume in patients with AF, even in the absence of cerebral infarcts.\(^2^5,2^6\) Cerebral microinfarctions (that may remain undetected by MRI) are neuropathological findings associated with dementia\(^2^7\); an association between AF and cortical microinfarcts has also been described.\(^2^8\) In patients with AF, microemboli may play a role in the accumulation of these microinfarcts and, thus, cognitive decline.\(^2^9\) Cerebral hypoperfusion due to decreased cardiac output and a proinflammatory state associated with atrial cardiopathy might worsen a coexistent neurodegenerative process.\(^7,2^4\) Comorbidities such as hypertension, diabetes mellitus, and hyperlipidemia lead to the development of cerebral microvascular disease and also are all known risk factors for both AF and dementia.\(^3^0,3^1\)

This study also showed that high AI-ECG-AF score (>0.50) was associated with presence of infarcts after adjusting for age and sex in participants with ECG showing sinus rhythm; however, this association did not remain when participants with AF were excluded. Additionally, the majority of infarcts observed were subcortical rather than embolic, as would be expected if the infarcts were solely attributable to AF. These observations may be due to AI-ECG detection of markers of non-AF cardiac pathology, which are also related to small vessel cerebrovascular disease and cognitive decline.

Although the AI-ECG was trained to detect AF risk from ECGs acquired during normal rhythm, the biological factors that lead to the subtle, multiple, nonlinear ECG changes detected by the convolutional neural network are not known. Even in the absence of AF, vascular inflammation, electrophysiologic channels impacting depolarization or repolarization, metabolic changes affecting cell-to-cell electrical-signal transmission, and other factors may lead to the ECG changes detected by the AI-ECG. Atrial fibrillation and cognitive decline may share

---

**FIGURE 3.** High-threshold artificial intelligence—enabled electrocardiogram—atrial fibrillation (AI-ECG-AF) probability score (>0.5) is associated with presence of cerebral infarcts on magnetic resonance imaging in the unadjusted dichotomized model (A) and after adjusting for age and sex (B).
sufficient common biological precursors that the AI-ECG predicts cognitive decline in individuals who may never experience AF. The frequent nature of silent AF and incomplete monitoring to document AF makes answering this question difficult.

In our cohort, higher AI-ECG-AF scores correlated with future decline in global cognition and attention, but not other cognitive domains. This is in keeping with the most common pattern of cognitive impairment attributable to cerebrovascular disease, which preferentially affects processing speed and aspects of executive functioning but typically spares memory and language. Subcortical white-matter hyperintensities are associated with dementia related to cerebrovascular disease. Although white-matter hyperintensities are not independently associated with AF, subcortical strokes were the predominant type of infarct identified in our study participants.

Whether high probability of AF on AI-ECG can be considered a surrogate marker of AF and prompt anticoagulation for stroke prevention remains to be defined. When analyzed as a continuous variable, the AI-ECG-AF score was associated with cognitive decline but not with infarction on brain MRI, suggesting that cognitive decline may be a more sensitive endpoint than radiological infarctions (including silent infarctions) for evaluating the effect of anticoagulation in patients with high risk of AF. Whether initiation of anticoagulation prevents future cognitive decline in patients with documented AF remains presently unknown. However, the need for inexpensive, easy-to-obtain risk markers to identify potential candidates for early intervention is increasingly urgent as new anticoagulation and anti-dementia therapies are developed. Because the ECG is inexpensive, ubiquitous, and integrated into medical workflows, the AI-ECG is an attractive screening option.

Strengths of this study include the large cohort size from a population-based study and the longitudinal analysis of cognitive data. Limitations of the study must also be acknowledged. The participants included in this study were mostly older; thus, the results cannot be extrapolated to younger individuals. For the dichotomized analyses of AI-ECG-AF score and infarcts, power was limited by only a small number of participants having a high-threshold AI-ECG-AF score. Duration of follow-up varied across participants, and we did not examine whether the associations of AI-ECG-AF scores with radiological infarction increased among participants with longer follow-ups or more than a single MRI. Participants underwent 3T 2D FLAIR MRI scans, but this may have underestimated the number of infarcts compared with 3D FLAIR MRI scans, which may be more sensitive. We assessed only the baseline AI-ECG, but there may be a role for serial testing to understand study risk over time. Future analyses could also include review of whether patients with elevated AI-ECG-AF score went on to develop AF.

CONCLUSION
An AI-ECG algorithm that indicates the presence of undiagnosed paroxysmal AF is associated with greater risk of cognitive decline. A high probability (>0.50) of AF on AI-ECG was also associated with presence of cerebral infarctions on MRI in participants with ECG showing sinus rhythm. The majority of infarcts observed were subcortical, suggesting that AI-ECG may not only be predictive of AF, but it also may detect other markers of non-AF cardiac disease which may share associations with small vessel cerebrovascular disease. Prospective, controlled studies are necessary to determine whether a high AF score is a biomarker to select patients for anticoagulation or more aggressive stroke risk factor modification to prevent cognitive impairment or cerebral infarcts.

Abbreviations and Acronyms: AF, atrial fibrillation; AI-ECG, artificial intelligence—enabled electrocardiogram; FLAIR, fluid attenuation inversion recovery; MCSA, Mayo Clinic Study of Aging

AI-ECG IDENTIFIES STROKE RISK, COGNITIVE DECLINE

(C.L.L., W.K.K., M.M.M.), Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery (XY), Department of Radiology (P.V., C.R.J.), and the Department of Psychiatry and Psychology (M.M.M.), Mayo Clinic, Rochester, MN, USA.

Potential Competing Interests: Dr Noseworthy has received grants from the National Institute on Aging of the National Institutes of Health (NIH) under Award Number R01AG062436, the National Heart, Lung, and Blood Institute [NHLBI], the Agency for Healthcare Research and Quality (AHRQ), US Food and Drug Administration (FDA), and the American Heart Association (AHA); is a study investigator in an ablation trial sponsored by Medtronic; with Mayo Clinic is involved in a potential equity/royalty relationship with AliveCor; has served on an expert advisory panel for Optum; and with Mayo Clinic has filed patents related to the application of AI to the ECG for diagnosis and risk stratification. Drs Noseworthy, Friedman, and Attia are co-inventors of the AI ECG algorithm described in this manuscript which has been licensed to Anuman whereby they and Mayo Clinic may receive financial benefit from its use in the future. Dr Kremers has received grants from AstraZeneca, Biogen, and Roche. Dr Mielke has received consulting fees from Biogen and Brain Protection Company; and has received speaking fees from Miller Medical Communications LLC. Dr Jack serves on an independent data monitoring board for Roche and has consulted for Eisai and Lilly, but he receives no personal compensation from any commercial entity; and he has received grants from NIH and the Alexander Family Alzheimer’s Disease Research Professorship of the Mayo Clinic. Dr Machulda has received grants from the NIH and DOD. Dr Vemuri has received grants from the NIH; and has received speaking fees from Miller Medical Communications LLC. Dr Jack serves on an independent data monitoring board for Roche and has consulted for Eisai and Lilly, but he receives no personal compensation from any commercial entity; and he has received grants from NIH and the Alexander Family Alzheimer’s Disease Research Professorship of the Mayo Clinic. Dr Machulda has received grants from the NIH. Dr Knopman has served on a Data Safety Monitoring Board for the DIAN study; serves on a Data Safety monitoring Board for a tau clinical trial sponsored by Lilly Pharmaceuticals and the University of Southern California; he serves as a consultant for Biogen and Biogen Inc, Eli Lilly and Company, and Genentech Inc has received publishing royalties for Mild Cognitive Impairment (Oxford University Press, 2003); and has received research support from the NIH and the Robert H. and Clarice Smith and Abigail Van Buren Alzheimer’s Disease Research Program of the Mayo Foundation. Dr Graff-Radford has received grants from the National Institute on Aging of the National Institutes of Health (NIH) under Award Number K76AG057015 and serves on the editorial board of Neurology. The remaining authors report no potential competing interests.

Grant Support: Research reported in this publication was supported by the National Institute on Aging of the National Institutes of Health (NIH) under Award Number K76AG057015 and the NIH Grants R01 AG01378 (Dr Jack) Evaluating and Extending Our Hypothetical Model of Alzheimer’s Biomarkers; R01 AG041851 (Drs Jack and Knopman) Validating the New Criteria for Preclinical Alzheimer’s disease; U01 AG006786 (Dr Petersen) — Mayo Clinic Study of Aging (MCSA); R01 NS079495 (Dr Vemuri) Development, Validation, and Application of an Imaging based CVD Scale; P30 AG062677 (Dr Petersen) Alzheimer’s Disease Research Center (ADRC), and the GHR Foundation. This study was made possible by the Rochester Epidemiology Project (grant number R01-AG034676). The funders had no role in the conception or preparation of this manuscript.

Correspondence: Address to Jonathan Graff-Radford, MD, Department of Neurology, Mayo Clinic College of Medicine, 200 1st Street SW, Rochester, MN 55905 USA (Graff-Radford@mayo.edu; Twitter: @j_graffradford).

ORCID
Camden L. Lopez: https://orcid.org/0000-0003-4516-8088; Alejandro A. Rabinstein: https://orcid.org/0000-0001-8359-2838; Michelle M. Mielke: https://orcid.org/0000-0001-7177-1185; Clifford R. Jack: https://orcid.org/0000-0001-7916-622X; Mary M. Machulda: https://orcid.org/0000-0003-4834-5967; David S. Knopman: https://orcid.org/0000-0002-6544-066X; Jonathan Graff-Radford: https://orcid.org/0000-0003-2770-0691

REFERENCES
fibrillation as determined by brain magnetic resonance imaging. Am J Cardiol. 2016;113(4):655-661.


