Self-Reported Atrial Fibrillation and Risk of Stroke in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study

Elsayed Z. Soliman, MD, MSc, MS; George Howard, DrPH; James F. Meschia, MD; Mary Cushman, MD; Paul Muntner, PhD; Patrick M. Pullicino, MD; Leslie A. McClure, PhD; Suzanne Judd, PhD; Virginia J. Howard, PhD

Background and Purpose—We compared the associations of self-reported atrial fibrillation (AF) and ECG-detected AF with incident stroke in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study.

Methods—In this analysis, 27,109 participants aged 45 years or older without previous stroke were included. Incident stroke was defined by different methods.

Results—After adjustment for components of the FSRS, self-reported AF, ECG-detected AF, and AF by either method were predictive of incident stroke (HR, 1.41; 95% CI, 1.05–1.88; HR, 1.90; 95% CI, 1.10–3.27; HR, 1.53; 95% CI, 1.16–2.01, respectively). When self-report, ECG, or either method, separately, were considered as the method of AF ascertainment in the FSRS, the HR per 1% increase in the FSRS were identical across AF ascertainment methods (HR, 1.04; 95% CI, 1.03–1.04; HR, 1.04; 95% CI, 1.04–1.05; HR, 1.04; 95% CI, 1.03–1.04; respectively).

Conclusions—Self-reported AF is a strong predictor of stroke that can be used interchangeably or in combination with ECG-detected AF in stroke risk prediction models. (Stroke. 2011;42:2950-2953.)

Key Words: atrial fibrillation ■ electrocardiography ■ self-reported atrial fibrillation

Atrial fibrillation (AF) is a major risk factor for stroke. Electrocardiogram (ECG) and self-reported history of a physician diagnosis are the most commonly used methods for detecting this serious arrhythmia in population studies. Nevertheless, the usefulness of self-reported AF data are often called into question because of the possibility of unreliability.

Several studies attempted to assess the validity of self-reported cardiovascular diseases by comparing self-reports with medical records. The challenge in applying this validation approach to AF is its paroxysmal (intermittent) nature in 40% of cases. Because the clinical significance of detecting AF relates mainly to identifying those at increased stroke risk, demonstrating that self-reported AF is an equivalent stroke risk factor to ECG-detected AF would provide validation of self-reported data.

Materials and Methods

The goals and design of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, a U.S. national longitudinal study, have been published. REGARDS was designed to investigate causes of regional and racial disparities in stroke mortality, oversampling blacks and residents of the southeastern “stroke belt region.” Individuals were recruited from a commercially available list of residents using mail and telephone contact, with a 49% cooperation rate. Demographic information and medical history were obtained by telephone interview. All methods were approved by Institutional Human Subjects Review Boards. A brief physical examination was conducted 3 to 4 weeks after the telephone interview, including standardized measurements of risk factors, collection of blood and urine, and recording of resting ECG.

Participants are followed-up every 6 months by telephone for possible stroke outcomes. Of 30,239 REGARDS participants enrolled between 2003 and 2007, 29,648 had follow-up data. Of these, we excluded 1886 participants reporting previous stroke, 331 not answering questions on self-reported AF, and 322 without an ECG.

AF Ascertainment

Information on AF ascertainment was previously published. Briefly, self-reported AF was defined as a positive response to the question, “Has a physician or a health professional ever told you that you had atrial fibrillation?” ECG-detected AF was identified from
the baseline ECGs, which were centrally read by electrocardiographers blinded to clinical data.

### Stroke Events

Details on stroke events adjudication have been previously published. In summary, reports of possible stroke during follow-up generated a request for retrieval of medical records that were centrally adjudicated by physicians. Stroke events were defined following the World Health Organization definition. Events not meeting the World Health Organization definition but with symptoms lasting <24 hours with neuroimaging consistent with acute ischemia or hemorrhage were classified as "clinical strokes." This analysis included World Health Organization-defined and clinical ischemic stroke cases.

### Statistical Analysis

Cox proportional hazards analysis was used to examine the hazard ratios (HR) and 95% confidence interval (CI) for incident stroke associated with self-reported AF, ECG-detected AF, and AF by either method, separately. Models were adjusted for age, sex, and race (demographic models), and then further adjusted for components of the Framingham Stroke Risk Score (FSRS; Framingham models), which included use of antihypertensive drugs, systolic blood pressure, current smoking, diabetes, left ventricular hypertrophy, and previous heart disease. In additional models, we examined effects of including socioeconomic status and warfarin use in the Framingham models. We examined the effect of the method of AF ascertainment on the predictive ability of the FSRS. To reduce potential biases because of missing data and to improve precision, we applied multiple imputation techniques to classify potential stroke events still in process and for medical records that could not be retrieved (≈10% each; details are available elsewhere).

### Results

There were 27,109 participants (45% males, 40% blacks) included in this analysis. AF was detected by self-report in 2084 participants, by ECG in 360, and by both methods in 222. Table 1 shows participant characteristics by the method of AF ascertainment.

During a mean follow-up of 4.4 years, 378 strokes occurred. The Figure shows the stroke-free survival curves by AF detection.

In Table 2, self-reported AF, ECG-detected AF, and AF by either method were predictive of stroke in all models, with a slightly higher HR for ECG-detected AF. Adding socioeconomic status to the Framingham models did not substantially change the HR associated with self-reported AF (HR, 1.41; 95% CI, 1.05–1.88; \( P = 0.022 \)) or ECG-detected AF (HR, 1.88; 95% CI, 1.09–3.25; \( P = 0.023 \)) compared to the Framingham models in Table 2. However, adding warfarin use to the Framingham model attenuated the HR for incident stroke associated with both self-reported AF (HR, 1.30; 95% CI, 0.95–1.77; \( P = 0.10 \)) and ECG-detected AF (HR, 1.52; 95% CI, 0.81–2.86; \( P = 0.19 \)).

When self-report, ECG, or either method, separately, were considered as the method of AF ascertainment in the FSRS, the HR per 1% increase in the FSRS were identical for each AF ascertainment method (HR, 1.04; 95% CI, 1.03–1.04; HR, 1.04; 95% CI, 1.04–1.05; HR, 1.04; 95% CI, 1.03–1.04; respectively; \( P < 0.001 \) for all). There were no meaningful differences in observed associations when we stratified the analyses by race or sex (data not shown).

### Discussion

In this analysis, self-reported AF was a strong independent risk factor for stroke. We also showed that self-reported AF can be used interchangeably with ECG-detected AF for stroke risk prediction using the FSRS. These findings suggest that important predictive information can be derived from a simple AF ascertainment method: self-report of a previous physician diagnosis. Adjustment for warfarin use in this analysis attenuated the risk of stroke associated with self-reported AF and with ECG-detected AF. This means that self-reported AF may be not only an independent risk factor
for stroke but also a modifiable risk factor if treated in a manner similar to the ECG-AF. However, the risk–benefit of routine use of warfarin in patients with self-reported AF without ECG evidence needs to be evaluated in future studies.

Based on our findings, we propose that self-reported AF and/or ECG-detected AF would be a good choice if both methods are available. Compared to ECG or self-report alone, using a classification such as “either” was a good predictor in this study in terms of HR and significance/precision (P and CI). However, in case of unavailable ECG data, self-reported AF could be a useful predictor that provides important information.

So, why is self-reported AF a strong risk factor for stroke despite the possibility of misclassification because of inaccuracy of reporting medical history? An explanation can be derived from the possible reasons why an individual may wrongfully report having AF. It is possible that positive reports for AF could be triggered by history of other arrhythmias or heart disease that are recollected as AF. Because history of heart disease and arrhythmias are risk factors for stroke, it is not surprising that self-reported AF has prognostic significance, even if not true in all cases. Further, results from the Cardiovascular Health Study showed that self-reported AF has similar associations with risk factors and medication use as ECG-detected AF, so it is plausible that self-reported AF could have a similar prognostic significance as ECG.

Our study has some limitations. We validated self-reported AF in terms of prognostic significance, not diagnostic accuracy. This enabled us to comment on the usefulness of self-reported AF as a predictor for stroke. We could not confirm the appropriateness of self-reported AF to estimate prevalence of AF. Nevertheless, we previously reported that combining data from self-report and ECG provided more logical estimates for the racial distribution of AF that partially explain the paradox of high stroke and low reported prevalence of AF in blacks. Two additional limitations of our study is that we examined the usefulness of self-reported AF in the context of the FSRS, which was developed in whites, not in blacks. However, we stratified the results by race and examined interactions, and there were no meaningful black–white differences. Finally, the REGARDS population was collected from a commercial listing, which means that more affluent might have been over-represented, and given the relatively low cooperation rate, the generalizability of our findings might have been affected. Despite these limitations, our study answered a number of questions related to the validity of self-reported AF using a novel validation approach in a well-defined large biracial cohort.

Conclusions

In conclusion, self-reported AF is a strong predictor for stroke that can be used interchangeably or in combination with ECG-detected AF in stroke risk prediction models. These findings support using self-report as a method for AF ascertainment.

Table 2. Association Between Atrial Fibrillation Identified Using Different Methods and Incident Stroke

<table>
<thead>
<tr>
<th>Method</th>
<th>Demographic Model HR (95% CI)</th>
<th>P-value</th>
<th>Framingham Model HR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported atrial fibrillation</td>
<td>1.55 (1.17–2.04)</td>
<td>0.002</td>
<td>1.41 (1.05–1.88)</td>
<td>0.020</td>
</tr>
<tr>
<td>ECG-detected atrial fibrillation</td>
<td>1.78 (1.03–3.09)</td>
<td>0.039</td>
<td>1.90 (1.10–3.27)</td>
<td>0.022</td>
</tr>
<tr>
<td>Atrial fibrillation by either self-report or ECG</td>
<td>1.66 (1.27–2.17)</td>
<td>&lt;0.001</td>
<td>1.53 (1.16–2.01)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; HR, hazard ratio; ECG, electrocardiogram.

*Demographic model plus use of antihypertensive medications, systolic blood pressure, current smoking, diabetes, left ventricular hypertrophy, and previous heart disease.
Acknowledgments
The authors thank the investigators, staff, and participants of the REGARDS study for their valuable contributions. A full list of REGARDS investigators and institutions can be found at http://www.regardsstudy.org.

Source of Funding
This research project is supported by a cooperative agreement U01 NS041588 from the National Institute of Neurological Disorders and Stroke, National Institutes of Health, Department of Health and Human Services.

Disclosures
None.

References
Self-Reported Atrial Fibrillation and Risk of Stroke in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study
Elsayed Z. Soliman, George Howard, James F. Meschia, Mary Cushman, Paul Muntner, Patrick M. Pullicino, Leslie A. McClure, Suzanne Judd and Virginia J. Howard

Stroke. 2011;42:2950-2953; originally published online August 4, 2011; doi: 10.1161/STROKEAHA.111.621367
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2011 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/42/10/2950

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/