Detection of Paroxysmal Atrial Fibrillation by 30-Day Event Monitoring in Cryptogenic Ischemic Stroke

The Stroke and Monitoring for PAF in Real Time (SMART) Registry

Alexander C. Flint, MD, PhD; Nader M. Banki, MD; Xiushui Ren, MD; Vivek A. Rao, MD; Alan S. Go, MD

Background and Purpose—Patients with cryptogenic ischemic stroke may have undetected paroxysmal atrial fibrillation (PAF). We established the Stroke and Monitoring for PAF in Real Time (SMART) Registry to determine the yield of 30-day outpatient PAF monitoring in cryptogenic ischemic stroke.

Methods—The SMART Registry was a 3-year, prospective multicenter registry of 239 patients with cryptogenic ischemic stroke undergoing 30-day outpatient autotriggered PAF detection in Kaiser Permanente Northern California.

Results—In intention-to-monitor analysis, PAF was detected in 29 of 239 patients (12.1%; 95% CI, 8.6%–16.9%). After retrospective chart review, a new diagnosis of PAF was confirmed in 26 of 236 patients (11.0%; 95% CI, 7.6%–15.7%). The majority of detected PAF events were asymptomatic; only 6 of 98 recorded PAF events (6.1%) were patient-triggered or associated with symptoms.

Conclusions—Approximately 1 in every 9 patients with cryptogenic ischemic stroke was found to have new PAF within 30 days. Routine monitoring in this population should be strongly considered. (Stroke. 2012;43:00-00.)

Key Words: atrial fibrillation

Atrial fibrillation (AF) is a risk for ischemic stroke.1 Patients with ischemic stroke with AF are, in the absence of specific contraindications, treated with anticoagulation for secondary stroke prevention.1

Patients with AF, whether paroxysmal or chronic,1 appear to have similar risks of ischemic stroke.2,3 Anticoagulation is superior to antiplatelet treatment for the prevention of ischemic stroke in both paroxysmal atrial fibrillation (PAF) and chronic AF.3,4

Undetected PAF may be the cause of some cases of cryptogenic ischemic stroke (CIS).5 Approximately 40% of patients with ischemic stroke have no discernible cause found on initial workup and are considered to have CIS.6 Several small studies of long-term cardiac monitoring have suggested that 5% to 20% of patients with CIS may have PAF as a likely contributing cause.5

We established the Stroke and Monitoring for Atrial fibrillation in Real Time (SMART) Registry to determine of the yield of long-term cardiac event recording in CIS.

Patients and Methods

The SMART Registry was a prospective multicenter cohort study to examine the yield of 30-day outpatient cardiac monitoring for PAF in patients with CIS. Patients were enrolled in the SMART Registry from June 1, 2008, to May 31, 2011, when a neurologist at any of the participating hospitals or clinics in Kaiser Permanente Northern California referred a patient with CIS for 30-day outpatient cardiac monitoring by way of a web-based consult referral system. The referral system provided decision support that described the inclusion/exclusion criteria of the SMART Registry. Listed inclusion criteria included a recent diagnosis of ischemic stroke with a negative stroke etiology workup. Excluded specific causes of stroke included known AF, carotid stenosis ≥70% on the symptomatic side, lacunar/small vessel syndrome, and either aortic arch plaque or intracranial atherosclerosis felt to be the cause of the patient’s stroke.

Thirty-day outpatient electrocardiographic loop recording was performed with the CardioPAL SAVI (Medicomp, Inc, Melbourne, FL). Monitors were mailed to the patient’s home; hookup and maintenance were performed by telephone. Events were autocaptured from cardiac rhythm state changes or by button press. All recorded events were initially reviewed by a study physician (A.C.F.) and then device-detected possible or probable PAF events were independently adjudicated by 2 board-certified Cardiologists (N.B. and X.R.) using standard electrocardiographic criteria for AF and a minimum event duration of 5 seconds. Secondary analysis determined the number of patients with a minimum event duration of 30 seconds. Events adjudicated as PAF by both study cardiologists were counted as a positive study.

We used Stata Version 10 (StataCorp, College Station, TX) for statistical analysis. Comparisons of continuous variables were made using the Mann-Whitney U test; comparisons of categorical data were made using Fisher exact test; and 95% CIs were determined by the Wilson formula.

Received May 29, 2012; final revision received June 26, 2012; accepted June 28, 2012.

From the Departments of Neuroscience (A.C.F., V.A.R.) and Cardiology (N.M.B., X.R.), Kaiser Permanente, Redwood City, Redwood City, CA; the Division of Research, Kaiser Permanente Northern California, Oakland, CA (A.S.G.); and the Departments of Epidemiology, Biostatistics and Medicine, University of California, San Francisco, San Francisco, CA (A.S.G.).

Correspondence to Alexander C. Flint, MD, PhD, Kaiser Permanente, Redwood City, Department of Neuroscience, 1150 Veterans Boulevard, Redwood City CA 94063. E-mail alexander.c.flint@kp.org

© 2012 American Heart Association, Inc.

Stroke is available at http://stroke.ahajournals.org

DOI: 10.1161/STROKEAHA.112.665844
The Institutional Review Board of the Kaiser Foundation Research Institute approved this study with waiver of informed consent.

Results

Three hundred thirty-four study orders were placed, and 239 patients (71.6%) completed a loop recorder study. Monitors were worn for 24.5/8.7 days. PAF was detected in 29 patients (12.1%; 95% CI, 8.3%–16.9%), and PAF episodes 30 seconds were seen in 16 patients (6.7%; 95% CI, 3.9%–10.6%). After 3 patients were identified with prior evidence of PAF based on retrospective chart review, a new diagnosis of PAF was made in 26 of 236 patients (11.0%; 95% CI, 7.6%–15.7%). In 2 patients, both PAF and atrial flutter were detected. Monitoring duration was similar between patients with or without detected PAF (median, 28 versus 28 days; P = 0.61). We did not detect significant differences in patient characteristics between those with or without PAF (Table).

In patients with PAF, the first episode was recorded an average of 11.4/8.6 days after initiation of monitoring with a median of 2 (interquartile range, 1–3) events detected per patient. Twenty-four percent of events were detected late in the 30-day window (Figure). Most PAF events were asymptomatic; only 6 of 98 PAF events (6.1%) were from a patient-triggered recording or were associated with patient-reported symptoms.

Discussion and Conclusion

This is the largest multicenter registry to date of long-term, outpatient monitoring for PAF among patients with CIS. The yield of the test (11%–12%) suggests that many patients with CIS may have undiscovered PAF. Based on the estimated 5.8 million people in the United States with a history of stroke and the prevalence of CIS, our results suggest that approximately 200,000 patients in the United States may have CIS associated with PAF.

The majority (approximately 94%) of PAF events in our study were subclinical and thus would have been missed without autotriggered AF monitoring. Recent data from patients with implanted pacemakers or implantable cardioverter defibrillators have confirmed the risk of stroke with subclinical AF. Also, many PAF events in our study were detected late in the 30-day recording window, underscoring the need for prolonged monitoring in this population.

Our study has limitations. Other monitoring methods (such as implanted PAF monitors) or study designs (such as a single center with rigid control over stroke workup testing) might

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n=239)</th>
<th>PAF (n=29)</th>
<th>No PAF (n=210)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.6±13.8</td>
<td>69.3±11.3</td>
<td>64.0±14.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Female</td>
<td>39.5%</td>
<td>35.7%</td>
<td>40.0%</td>
<td>0.84</td>
</tr>
<tr>
<td>NIHSS</td>
<td>2 (1–4)</td>
<td>2 (1–3.25)</td>
<td>2 (1–4)</td>
<td>0.52</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>79.5%</td>
<td>72.4%</td>
<td>80.5%</td>
<td>0.33</td>
</tr>
<tr>
<td>Black</td>
<td>6.3%</td>
<td>6.9%</td>
<td>6.2%</td>
<td>0.70</td>
</tr>
<tr>
<td>Asian</td>
<td>12.1%</td>
<td>13.8%</td>
<td>11.9%</td>
<td>0.76</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.7%</td>
<td>3.5%</td>
<td>12.9%</td>
<td>0.22</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>1.3%</td>
<td>3.5%</td>
<td>1.0%</td>
<td>0.32</td>
</tr>
<tr>
<td>Prior stroke or TIA</td>
<td>18.8%</td>
<td>10.3%</td>
<td>20.0%</td>
<td>0.31</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>10.5%</td>
<td>3.5%</td>
<td>11.4%</td>
<td>0.33</td>
</tr>
<tr>
<td>Chronic heart failure</td>
<td>4.6%</td>
<td>7.1%</td>
<td>4.3%</td>
<td>0.62</td>
</tr>
<tr>
<td>Hypertension</td>
<td>66.0%</td>
<td>75.0%</td>
<td>64.8%</td>
<td>0.40</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>14.7%</td>
<td>25.0%</td>
<td>13.3%</td>
<td>0.15</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>90.8%</td>
<td>92.9%</td>
<td>90.5%</td>
<td>0.99</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol, mg/dL</td>
<td>105.7±37.1</td>
<td>107.2±28.5</td>
<td>105.6±38.0</td>
<td>0.86</td>
</tr>
<tr>
<td>Time from stroke to monitoring, d</td>
<td>29 (17–50)</td>
<td>26 (17–43)</td>
<td>30 (17–51)</td>
<td>0.44</td>
</tr>
<tr>
<td>Duration of monitoring, d</td>
<td>28 (20–30)</td>
<td>28 (23–30)</td>
<td>28 (18–30)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Continuous measures are presented as mean±SD or as median (interquartile range) with P values from the Mann-Whitney U test. Categorical measures are presented as percent of total in each category with P values from Fisher exact test.

PAF indicates paroxysmal atrial fibrillation; NIHSS, National Institutes of Health Stroke Scale; Prior stroke or TIA, history of ischemic stroke or transient ischemic attack before the stroke that prompted the PAF monitoring study; Cardiovascular disease, history of myocardial infarction, unstable angina, percutaneous coronary intervention, or coronary artery bypass graft surgery.

Figure. Time to first PAF detection. Distribution of first PAF events stratified by 10-day epochs (first, second, and last). Percentage of total first PAF events in each bin is shown overlying the graph. PAF indicates paroxysmal atrial fibrillation.
have detected a higher incidence of PAF. We do not have data on how many patients were “prescreened” with inpatient telemetry. We did not include or exclude patients on the basis of echocardiographic findings. The 90-second recording epoch of the used device prevented a meaningful analysis of PAF event duration. We did not clinically link PAF detection to anticoagulation, and it remains to be proven that the specific group of patients with CIS with PAF would have the same benefit from anticoagulation as seen in large randomized controlled trials of anticoagulation for AF.

Our results, taken together with similar results in smaller studies, suggest that the yield of 30-day monitoring for PAF in CIS is high enough to merit consideration of routine testing in this patient population.

Sources of Funding
Monitoring was purchased from Medicomp, Inc (Melbourne, FL) as part of clinical care in Kaiser Permanente Northern California. The study was designed and run by the principal investigator (Dr Flint).

Disclosures
None.

References
Detection of Paroxysmal Atrial Fibrillation by 30-Day Event Monitoring in Cryptogenic Ischemic Stroke: The Stroke and Monitoring for PAF in Real Time (SMART) Registry
Alexander C. Flint, Nader M. Banki, Xiushui Ren, Vivek A. Rao and Alan S. Go

Stroke. published online August 7, 2012;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 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/early/2012/08/10/STROKEAHA.112.665844

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/