Predictive Value of Newly Detected Atrial Fibrillation Paroxysms in Patients With Acute Ischemic Stroke, for Atrial Fibrillation After 90 Days

Peter Higgins, MRCP; Jesse Dawson, MD; Peter W. MacFarlane, DSc; Kate McArthur, MRCP; Peter Langhorne, PhD; Kennedy R. Lees, MD

Atrial fibrillation (AF) may arise de novo as a complication of acute ischemic stroke (AIS). Differentiation between patients with AF antecedent to stroke and those with new onset AF is not feasible. If such new onset episodes are only transient, they may confer no subsequent risk and need not prompt long-term anticoagulation. Evidence of AF at clinical presentation derived from a 12-lead ECG may thus represent a transient phenomenon. However, such evidence of AF was the basis for the inclusion of the majority of patients enrolled in secondary preventative studies that have demonstrated benefit of anticoagulant therapy. Although we have data that suggest that patients diagnosed with AF from an admission 12-lead ECG are likely to continue to exhibit AF long after the acute neurological injury, we lack information on the predictive value of paroxysmal AF (PAF) identification through extended cardiac event monitoring in the immediate aftermath of stroke.

Intensive and extended cardiac event monitoring immediately after stroke increases detection of PAF episodes of both sustained duration, which would justify consideration of anticoagulant-based secondary prevention, and of briefer duration, of less clear significance. We evaluated the predictive value of AF detection immediately after AIS or transient ischemic attack, for subsequent AF detection through noninvasive cardiac event monitoring, repeated after 90 days. This should inform therapeutic decisions based on PAF detected in the period immediately after acute stroke, which has been criticized as a measure of long-term risk.

Methods

Study Design and Population

This was an observational substudy extension of a previously reported randomized controlled trial (ISRCTN 97412358), which evaluated the addition of 7 days of extended noninvasive cardiac event monitoring with an R-test device (AM) to guideline-based standard practice (SP) investigation for PAF after ischemic stroke and transient ischemic attack. Details of the study population, recruitment, cardiac event monitoring technology, and study outcomes are reported elsewhere. In brief, we investigated 49 patients within 7 days of AIS for PAF according to current guidelines; 23 patients received 7 days of additional noninvasive cardiac event monitoring with an R-test device early after their stroke (ISRCTN 97412358). Ninety days after AIS, everyone underwent 7 days of cardiac event monitoring. We calculated the PPV and NPV of immediate PAF detection through extended cardiac event monitoring and through any investigative modality, for the presence of PAF on the 90-day event monitor.

Results

PAF detected by a 7-day event monitor within 2 weeks of AIS had a PPV of 100% (95% confidence interval, 72%–100%) for PAF confirmation after 90 days. NPV after 7 days of event monitoring was 64% (95% confidence interval, 35%–87%). PAF detected early by any modality had a PPV of 100% (95% confidence interval, 76%–100%). However, the NPV in the absence of R-test monitoring was only 42% (95% confidence interval, 28%–58%).

Conclusions

AF detection through any means immediately after stroke holds strong PPV for confirmation after 90 days, justifying treatment decisions on early monitoring alone. However, failure to identify AF through early monitoring has only modest NPV even after 7 days of monitoring; repeated investigation is desirable. 

Key Words: atrial fibrillation ■ ischemic attack, transient ■ stroke

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event monitoring methodology, and end point assessment have been reported previously. All participants, irrespective of randomization group, were invited to attend for 7 days of noninvasive cardiac event monitoring 90 days after their enrolment in the trial.

Follow-Up
After 90 days, consenting patients underwent another 7-day monitoring period; methods were as described previously. Rhythm strips were reviewed and any AF episodes were categorized as either sustained (episodes >20 s) or nonsustained (episodes >6 conducted ventricular beats but <20 s) duration; the combination of either was reported as episodes of any duration.

Statistical Analysis
Comparison of AF detection between initial investigations and the 90-day analysis was performed considering the interval analysis as the gold standard measurement, being performed under stable conditions remote from any stressors associated with the acute stroke. The positive predictive value (PPV) and negative predictive value, together with 95% confidence intervals, were calculated for AF episodes detected by each of 7 days of duration early noninvasive cardiac event monitoring; guideline-based SP investigations for PAF; any investigative modality combined. Predictive value was calculated for detection of any duration and sustained duration PAF episodes, for episodes of corresponding duration on subsequent monitoring. The predictive value of nonsustained duration episodes for subsequent sustained duration episodes was also assessed. Minitab (version 16) was used to perform statistical analysis.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66.73 (9.19)</td>
</tr>
<tr>
<td>Stroke to randomization; median (IQR)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>NIHSS (stroke patients only); median (IQR)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>152.7 (25.9)</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>79.2 (13.1)</td>
</tr>
<tr>
<td>Heart rate</td>
<td>77.0 (17.1)</td>
</tr>
<tr>
<td>Male sex</td>
<td>51.0%</td>
</tr>
<tr>
<td>Qualifying event stroke</td>
<td>67.3%</td>
</tr>
<tr>
<td>Qualifying event TIA</td>
<td>32.7%</td>
</tr>
<tr>
<td>TACS</td>
<td>8.2%</td>
</tr>
<tr>
<td>PACS</td>
<td>44.9%</td>
</tr>
<tr>
<td>LACS</td>
<td>32.7%</td>
</tr>
<tr>
<td>POCs</td>
<td>14.3%</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>18.4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>61.2%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16.3%</td>
</tr>
<tr>
<td>Smoker</td>
<td>28.6%</td>
</tr>
</tbody>
</table>

Continuous baseline characteristic values are quoted as mean (SD) unless otherwise stated; IQR indicates interquartile range; LACS, lacunar anterior circulation stroke; NIHSS, National Institutes of Health Stroke Scale; PACS, partial anterior circulation stroke; POCs, posterior circulation stroke; TACS, total anterior circulation stroke; and TIA, transient ischemic attack.

Results
Interval R-testing was performed in 49 of 100 patients, who were enrolled in the original trial (26 from the SP group and 23 from the SP-AM group). There was no technical failure among the interval R-tests. Baseline characteristics are detailed in Table 1. Baseline characteristics in patients who underwent interval R-test evaluation seemed balanced with those who did not, except that baseline National Institutes of Health Stroke Scale was lower and treatment with angiotensin converting enzyme inhibitor and calcium channel blocker were each higher among patients who underwent interval testing.

Paroxysms of AF of sustained duration were observed in 14 of 49 individuals with interval R-testing (7 patients in each of the SP and SP-AM groups). Of these 14 cases, 7 patients (5 in the SP group and 2 in the SP-AM group) had not had sustained paroxysms identified during the 90-day follow-up period during the original trial. In 13 of these patients, the episode duration was in excess of 30 s. Paroxysms of AF of any duration were observed in 30 of 49 individuals with interval R-testing (16 patients in the SP group and 14 patients in the SP-AM group). Of these 30 cases, 16 patients (13 from the SP group and 3 from the SP-AM group) had not had AF identified during the 90-day follow-up period during the original trial. Technical limitations of the existing R-test device precluded quantification of the total burden of AF.

Table 2 details the PPV and negative predictive value of sustained and any duration PAF episodes detected by, respectively, initial R-test in the SP-AM group; SP investigations at 14 days (in the combined groups); and any study 1 investigation at 14 days (in the combined groups), for corresponding duration PAF episodes detected on interval R-test. Table 3 provides the PPV and negative predictive value of nonsustained episodes for subsequent sustained duration PAF episodes on interval monitoring.

Discussion
Detection of AF episodes in the days immediately after AIS carries high PPV for detection of corresponding duration episodes after 90 days, irrespective of the investigation modality. Despite limitations of modest sample size and convenience sampling from a larger clinical trial population, this offers reassurance that treatment decisions based on the AF episodes detected immediately after ischemic stroke are justifiable.

However, negative predictive value with extended noninvasive cardiac event monitoring was modest and was
poor if only short duration monitoring was used. Patients potentially eligible for anticoagulation and in whom AF is not initially detected may benefit from interval monitoring. Detection of AF episodes of nonsustained duration carried poor PPV for more sustained duration episodes after 90 days. The clinical significance of such brief episodes of PAF, detectable immediately after ischemic stroke, remains uncertain.

We still do not know the patient characteristics that should prompt repeated interval monitoring or the long-term significance of brief episodes of AF after stroke.

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Disclosures

Dr. Dawson reports fees from Boehringer Ingelheim, Pfizer, and Bayer. Dr. Lees reports fees from Boehringer Ingelheim and honoraria from ACL, who hold data monitoring committee responsibility for a trial in stroke of undetected origin in which occult atrial fibrillation may be a contributory factor. The other authors report no conflicts.

References


Table 3. PPV and NPV of Nonsustained PAF Episodes Detected Through Early Investigation, for Sustained PAF Episodes After 90 Days

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-test</td>
<td>40 (5–85)</td>
<td>72 (47–90)</td>
</tr>
<tr>
<td>Standard practice investigations alone</td>
<td>0 (0–95)</td>
<td>71 (55–83)</td>
</tr>
<tr>
<td>Any investigation modality</td>
<td>33 (4–78)</td>
<td>72 (56–85)</td>
</tr>
</tbody>
</table>

Data are presented as % (95% confidence interval). NPV indicates negative predictive value; PAF, paroxysmal atrial fibrillation; and PPV, positive predictive value.
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