Insertable Cardiac Event Recorder in Detection of Atrial Fibrillation After Cryptogenic Stroke
An Audit Report

Thorleif Etgen, MD; Manfred Hochreiter, MD; Markus Mundel, MD; Thomas Freudenberger, MD

Background and Purpose—Atrial fibrillation (AF) is the most frequent risk factor in ischemic stroke but often remains undetected. We analyzed the value of insertable cardiac event recorder in detection of AF in a 1-year cohort of patients with cryptogenic ischemic stroke.

Methods—All patients with cryptogenic stroke and eligibility for oral anticoagulation were offered the insertion of a cardiac event recorder. Regular follow-up for 1 year recorded the incidence of AF.

Results—Of the 393 patients with ischemic stroke, 65 (16.5%) had a cryptogenic stroke, and in 22 eligible patients, an event recorder was inserted. After 1 year, in 6 of 22 patients (27.3%), AF was detected.

Conclusions—These preliminary data show that insertion of cardiac event recorder was eligible in approximately one third of patients with cryptogenic stroke and detected in approximately one quarter of these patients new AF. (Stroke. 2013;44:2007-2009.)

Key Words: atrial fibrillation ■ cryptogenic stroke ■ event recorder

In cryptogenic strokes that constitute up to one third of all ischemic strokes, no cause is established, despite thorough diagnostic workup. Recent data suggest that paroxysmal atrial fibrillation (AF) may significantly contribute to cryptogenic stroke because extended cardiac monitoring up to 30 days revealed paroxysmal AF in 20% to 23% of cryptogenic strokes.1,2

In our study, we systematically assessed the incidence of newly detected AF by insertable recorders within 1 year in patients with a cryptogenic stroke.

Materials and Methods
We recorded all patients with ischemic stroke admitted in the year 2011 to the stroke unit at Klinikum Traunstein, Bavaria, Germany, which is a community hospital taking care of ≥200000 people.3 Cryptogenic stroke was defined by lack of stroke after thorough evaluation,4 which included MRI, standard 12-lead ECG, 24- to 72-hour continuous stroke unit ECG monitoring plus ≥1 additional 24-hour Holter-ECG, extra- and transcranial neurosonography, echocardiography, including transesophageal echocardiography, computed tomography/MRI angiography, and laboratory screening for prothrombotic states in patients aged <55 years.

The Reveal XT is a small leadless insertable cardiac monitor that is equipped with a new AF detection algorithm, demonstrating an overall accuracy of 98.5% for detecting AF.5,6 All patients with cryptogenic stroke who were offered the implantation of this cardiac event recorder only if they were feasible for an oral anticoagulation and had no other exclusion criteria according to cryptogenic stroke and underlying atrial fibrillation (CRYSTAL-AF).4 AF duration of ≥6 minutes was registered.

The primary end point was the percentage of patients with new AF within 12 months. Secondary outcomes comprised the time to first documented AF and the value of the patient assistance device. We also analyzed whether excessive supraventricular ectopic activity (excessive supraventricular ectopic activity ≥30 supraventricular ectopic complexes/h or episodes with runs of ≥20 supraventricular ectopic complexes in Holter monitoring)7 or specific neuroimaging patterns (1 versus >1 vascular stroke territory) were associated with new AF.

This project was approved by the ethics committee of the Technische Universität München. All event recorder patients gave written informed consent for insertion, and they (if alive) provided informed consent for retrospective data analysis.

Statistical analysis was performed using Statistical Package for the Social Sciences software (SPSS version 20, Chicago, IL). P<0.05 was considered statistically significant.

Results
In 2011, 393 patients with ischemic stroke were admitted. In 319 (81.2%) patients, cause according to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria8 could be established: 78 (19.8%) large-artery atherosclerosis, 141 (35.9%) cardioembolism, 69 (17.6%) small-vessel occlusion, 17 (4.3%) other determined cause, and 14 (3.6%) concurrent cause. Undetermined cause consisted in 74 patients (18.8%), and reasons comprised incomplete evaluation (n=5) and death (n=4). Cryptogenic stroke was diagnosed in 65 patients (16.5%), and in 22 (33.8%) patients, an event recorder was implanted without any complications. The insertion was not

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From the Department of Neurology (T.E., M.H., T.F.), and Department of Cardiology (M.M.), Kliniken Südostbayern—Klinikum Traunstein, Traunstein, Germany; and Department of Psychiatry and Psychotherapy, Technische Universität München, München, Germany (T.E.).

Correspondence to Thorleif Etgen, MD, Department of Neurology, Kliniken Südostbayern—Klinikum Traunstein, Cuno-Niggl-Strasse 3, D-83278 Traunstein, Germany. E-mail thorleif.etgen@klinikum-traunstein.de

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considered feasible in the remaining 43 patients. Details are given in the patient flow chart (Figure).

After 1 year of follow-up, in 6 patients (27.3%), paroxysmal AF was detected, and secondary prophylaxis was changed to oral anticoagulation. There were no significant differences in basic characteristics and risk factors among the group of patients with and without new paroxysmal AF (Table). No new transient ischemic attack or stroke had occurred in any of the 22 patients.

In 4 (67%) of the 6 patients with newly diagnosed AF, AF was asymptomatic and was only discovered on a routine analysis of the recorder. Two patients (33%) noticed heart palpitations and used the patient’s assistant device. Excessive supraventricular ectopic activity or ischemic stroke in >1 vascular territory was not associated with the detection of paroxysmal AF.

Discussion

These preliminary data are the first reporting the results of a systematic assessment and analysis of the value of an insertable cardiac event recorder in the detection of paroxysmal AF after cryptogenic ischemic stroke. First, the real-life time setting of this study allows a rough estimation of the practical options in the use of insertable event recorders and may help in calculating a cost-benefit analysis. Approximately, one third of patients with cryptogenic stroke were feasible for further evaluation by event recorder, whereas two thirds were not suitable mostly because of contraindications for an oral anticoagulation. Among those with recorder, in approximately one quarter paroxysmal AF is detected. By this, a subsequent classification of stroke etiology reduced the portion of cryptogenic stroke by ≈10%.

Second, this study demonstrated that a close insertion to the stroke event is manageable in daily practice, which reduces the time frame without cardiac monitoring after cryptogenic stroke, although all patients with new AF experienced AF later than 2 months after their stroke. Third, the time to first new AF was on average ≈5 months after stroke, which underlines the importance of long-term cardiac monitoring in cases of suspected AF, although this is in slight contrast to other results, suggesting a more earlier occurrence of new AF after ischemic stroke.9

Our study also encompassed some differences compared with CRYSTAL-AF.4 First, we selected patients with an MRI-proven ischemia. Further focusing on patients with multiple areas of MRI ischemia in different vascular territories may even increase the likelihood of AF detection with event recorders, although this factor was not significant in our study.10 In contrast to CRYSTAL-AF, we also required mandatory Holter-ECG before inclusion to assess patients with possible high-risk cardiac embolic sources (excessive supraventricular ectopic activity),7 but again this did not influence our results. Further differences comprise our vigorous definition of cryptogenic stroke, which is in contrast to the variable definition according to the standard protocol of

### Table. Demography

<table>
<thead>
<tr>
<th></th>
<th>AF Positive (n=6)</th>
<th>AF Negative (n=16)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.8 (45.3–86.4)</td>
<td>60.0 (54.4–65.6)</td>
<td>0.373</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>4 (66.7%)</td>
<td>7 (43.8%)</td>
<td>0.338</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (66.7%)</td>
<td>10 (62.5%)</td>
<td>0.856</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0 (0%)</td>
<td>2 (12.5%)</td>
<td>0.364</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>4 (66.7%)</td>
<td>12 (80.0%)</td>
<td>0.696</td>
</tr>
<tr>
<td>Smoking</td>
<td>2 (33.3%)</td>
<td>5 (31.3%)</td>
<td>0.926</td>
</tr>
<tr>
<td>ESVEA in Holter-ECG</td>
<td>0 (0%)</td>
<td>3 (18.8%)</td>
<td>0.254</td>
</tr>
<tr>
<td>Neuroimaging &gt;1 embolic territory</td>
<td>1 (16.7%)</td>
<td>6 (37.5%)</td>
<td>0.350</td>
</tr>
<tr>
<td>Time stroke: insertion event recorder, d</td>
<td>8.5 (6.5–10.5)</td>
<td>9.9 (6.4–13.4)</td>
<td>0.624</td>
</tr>
<tr>
<td>Time insertion event recorder: AF detection, d</td>
<td>152.8 (61.6–244.1)</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Categorical variables: number (percentage) with P values calculated by χ² test. Continuous variables: mean (95% confidence interval) with P values calculated by ANOVA. AF indicates atrial fibrillation; ESVEA, excessive supraventricular ectopic activity; and n/a, not applicable.
the participating center and inclusion up to 2 months after the ischemic event.4

The present study also has some limitations. First, being only a single-center cohort study with a small number of patients, these results have to be verified in a larger population. Second, this study is of retrospective nature, which does not allow the comparison with detection of paroxysmal AF by standard arrhythmia methods. However, these standard methods are not clearly defined and depend on local procedures (e.g., repeated performance of 24-hour ECG, cardiac evaluation after subjective palpitations). Our limited data suggest that the majority of paroxysmal AF occurs unnoticed by the patient and might not be detected by repeated 24-hour ECG. Third, we used continuous stroke unit ECG monitoring for 24 to 72 hours, but this did not include an automated analysis of ECG monitoring, which has recently been shown to increase the detection rate of paroxysmal AF in patients with stroke.11

Last, by analyzing only AF duration \( \geq \) 6 minutes shorter, clinically relevant AF episodes such as a 5-minute paroxysm might have been missed.

Disclosures

None.

References


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