To Monitor or to Not Monitor for Paroxysmal Atrial Fibrillation After Transient Ischemic Attack or Stroke
This Is the Question
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See related article, p 520.

Approximately 25% of ischemic strokes cannot be classified as large-vessel disease, cardiac embolism, or small-vessel disease. This remaining entity is called cryptogenic stroke. Cryptogenic in this context can mean that the cause of the transient ischemic attack (TIA) or stroke could not be elucidated during the stay of the patient in the stroke unit or that there was incomplete or insufficient diagnostic testing. Several patients with so-called cryptogenic stroke might have paroxysmal atrial fibrillation (AF), which is not detected with standard 24-hour Holter monitoring on the stroke unit. The detection of AF has major implications for effective secondary stroke prevention. In patients with AF, anticoagulation with warfarin is clearly superior to aspirin, and the novel anticoagulants are at least as effective as warfarin if not superior with a comparable or lower rate of major bleeding complications.

Kishore et al in this issue of *Stroke* present results from a systematic literature review and meta-analysis investigating the detection rate of different ECG monitoring techniques to detect AF in patients who had a TIA or an ischemic stroke. They were able to analyze 32 observational or randomized studies with 5038 participants. The detection rate for AF was 11.5%, with a wide variation of methods used, observation time, and minimal duration of arrhythmia to be defined as AF.

This review raises a fundamental question in stroke medicine and secondary stroke prevention. There are 2 ways to deal with the problem of undetected AF in patients with TIA or ischemic stroke. One way is as described here, which is prolonged ECG monitoring. The uncertainty remains which monitoring technique and which duration of ECG monitoring are optimal in determining AF detection rates versus patient compliance and cost. Another approach would be a randomized trial of novel anticoagulants versus antiplatelet therapy in patients with cryptogenic stroke, excluding patients with lacunar stroke with minimal 24-Holter monitoring at baseline. Such a trial would assume that many cryptogenic strokes are embolic in nature and that the treatment with novel anticoagulants would be superior to antiplatelet treatment with a similar rate of major bleeds. If such a trial would be positive, there would no longer be a need for prolonged ECG monitoring.

I would like to address some other issues with respect to ECG monitoring after TIA or stroke.

1. A major issue is the question what duration of AF constitutes the diagnosis of AF and would be associated with an increased stroke risk. Most studies use a >30-second AF duration as a threshold. We do not know, however, whether 30 seconds of AF lead to an increased stroke rate. The Asymptomatic AF and Stroke Evaluation in Pacemaker Patients and the AF Reduction Atrial Pacing Trial (ASSERT) study used a 6-minute AF duration as a threshold. In an expert meeting on topics around AF and stroke prevention at the National Institutes of Health (NIH) last year, most participating cardiologists and neurologists agreed that a 6-minute AF duration threshold is sensible.

2. A major issue is the question of whether all patients with TIA or stroke should undergo prolonged ECG monitoring or only those with cryptogenic stroke. In the meta-analysis of Kishore et al, the AF detection rates were higher in selected (13.4%) versus unselected patients (6.2%). Detection of AF in unselected patients will most probably identify patients with ≥2 stroke causes. From a cost-saving aspect, ECG monitoring beyond 24 hours most probably is only cost-saving in selected patients.

3. Another critical issue is the ECG recording method. Holter monitoring is usually applied for 24 to 48 hours. ECG monitoring on stroke units with AF detection software is most frequently used for 72 hours. External loop recorders can be used for ≤30 days (with a dramatic reduction in compliance over time). The most expensive way to monitor ECGs during long periods of time is the use of implantable event recorders such as the REVEAL-XT. We eagerly await the results of the Cryptogenic Stroke and Underlying Atrial Fibrillation (CRYSTAL-AF) study, which randomized patients with cryptogenic stroke to implantation of an event recorder or standard care and followed patients for ≤3 years. The results will be presented at the American Heart Association stroke conference in San Diego in February 2014.

4. The authors could only describe that prolonged ECG recording increases the yield of AF detection. They were unable to identify a monitoring duration after which the detection rates flatten or reach a plateau.

5. Another way to use prolonged ECG monitoring in a more cost-effective way would be to consider the stroke pattern on computed tomography or MRI. If the pattern is suggestive of a cardioembolic source, prolonged ECG monitoring beyond 24 hours might be justified.
6. The authors point out the major shortcoming of their meta-analysis. Most of the studies were small and underpowered with wide confidence intervals. Many studies did not report the definition of AF duration and vascular risk factors at baseline. The most important shortcoming is the fact that most studies did not report whether AF detection had an effect on the decision to anticoagulate a patient.

In stroke research, we now have a consensus on how to perform animal and human studies in stroke treatment and prevention with definition of entry criteria, description of methods, use of controls and placebo, and definition of outcome parameters; thanks to the Stroke Therapy Academic Industry Roundtable (STAIR) initiative. For further studies on long-term ECG recording, a similar consensus would be desirable.

Disclosures
Dr Diener served on the Steering Committee of the CRYSTAL-AF study. He received honoraria for participation in clinical trials, contribution to advisory boards, or oral presentations from Abbott, Allergan, AstraZeneca, Bayer Vital, BMS, Boehringer Ingelheim, CoAxia, Corimmmun, Covidien, Daichii-Sankyo, D-Pharm, EV3, Fresenius, GlaxoSmithKline, Janssen-Cilag, Johnson & Johnson, Knoll, Lilly, MSD, Medtronic, MindFrame, Neurobiological Technologies, Novartis, Novo-Nordisk, Paion, Parke-Davis, Pfizer, Sanofi-Aventis, Schering-Plough, Servier, Solvay, Thrombogenics, WebMD Global, Wyeth, and Yamanouchi. Financial support for research projects was provided by AstraZeneca, GSK, Boehringer Ingelheim, Lundbeck, Novartis, Janssen-Cilag, Sanofi-Aventis, Syngis, and Talecris. The Department of Neurology at the University Duisburg-Essen received research grants from the German Research Council (DFG), German Ministry of Education and Research (BMBF), European Union, NIH, Bertelsmann Foundation, and Heinz-Nixdorf Foundation. Dr Diener has no ownership interest and does not own stocks of any pharmaceutical or medical device company.

References
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