NICE National Institute for Health and Care Excellence

Eyes on Evidence

Expert commentary on important new evidence

Detecting atrial fibrillation in people who have had a stroke

Two randomised controlled trials reported that long-term electrocardiogram monitoring was more effective at detecting atrial fibrillation than 24-hour or intermittent electrocardiogram monitoring in people who had experienced apparent cryptogenic stroke or transient ischaemic attack.

Overview: The term 'cryptogenic stroke' is used to describe the 30–40% of cases of stroke where no cause can be identified (Schulz and Rothwell et al. 2003). Atrial fibrillation is a form of sustained heart arrhythmia that is thought to be responsible for up to 1 in 6 cases of stroke and transient ischaemic attack (TIA).

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Atrial fibrillation is hard to identify because it is often intermittent (paroxysmal) and asymptomatic. Anticoagulation therapy can be used to lower the risk of stroke in people with atrial fibrillation, but it is generally not used unless atrial fibrillation has been formally identified.

Short-term electrocardiogram (ECG) monitoring can be used to detect atrial fibrillation, but this approach cannot identify paroxysmal fibrillation. Previous studies have suggested that monitoring heart rhythms for a longer period after ischemic stroke or TIA can improve detection of atrial fibrillation and ensure patients are offered anticoagulation therapy (Higgins et al. 2013).

Current advice: The NICE guideline on atrial fibrillation recommends performing manual pulse palpation to assess for the presence of an irregular pulse that may indicate underlying atrial fibrillation in people presenting with stroke or TIA. An ECG should be performed in all people, whether symptomatic or not, in whom atrial fibrillation is suspected on the basis of an irregular pulse. In people with suspected paroxysmal atrial fibrillation undetected by standard ECG recording:

- use a 24-hour ambulatory ECG monitor in those with suspected asymptomatic episodes or symptomatic episodes less than 24 hours apart
- use an event recorder ECG in those with symptomatic episodes more than 24 hours apart.

The guidance adds that the CHA_2DS_2-VASc stroke risk score should be used to assess stroke risk in people with symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation. Anticoagulation with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist should be considered in people with non-valvular atrial fibrillation and previous stroke or TIA.
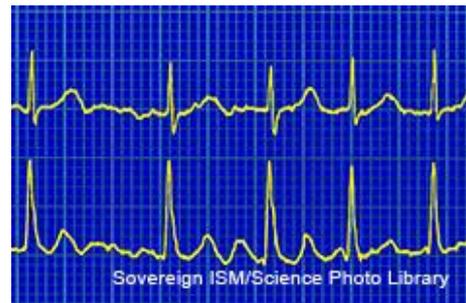
The NICE guideline on stroke adds that people with disabling ischaemic stroke who are in atrial fibrillation should be treated with aspirin 300 mg for the first 2 weeks before considering anticoagulation treatment.

The NICE Pathways on atrial fibrillation and stroke bring together all related NICE guidance and associated products on the conditions in sets of interactive topic-based diagrams.

New evidence: Two randomised controlled trials assessed long-term ECG monitoring to detect atrial fibrillation in people who had experienced a stroke or TIA and had no known atrial fibrillation.

Gladstone et al. (2014) enrolled people in Canada aged 55 years or older who had experienced a stroke and had no atrial fibrillation detected with conventional 24-hour screening. Participants were randomly assigned to ambulatory ECG monitoring either for 30 days with an event recorder or for 24 hours with a Holter monitor.

A total of 572 participants were randomised (287 to the 30-day monitoring group and 285 to the 24-hour monitoring group), and 557 (97.7%) were included in the intention-to-treat analyses. ECG monitoring for 30 days identified more people with atrial fibrillation (45 people, 16.1%) than 24-hour ECG monitoring (9 people, 3.2%; absolute difference=12.9 percentage points, 95% confidence interval [CI] 8.0 to 17.6 percentage points, $p<0.001$). By 90 days, patients in the 30-day monitoring group were more likely to be on anticoagulation therapy (18.6%, up from 5.6% at baseline) than were those in the 24-hour monitoring group (11.1%, up from 6.7%).

Sanna et al. (2014) enrolled people aged 40 years or older with stroke or TIA and no evidence of atrial fibrillation from Europe, Canada and the USA. Participants were randomly assigned to continuous ECG monitoring with an implantable subcutaneous cardiac monitor or to standard arrhythmia monitoring (ECG monitoring performed at study visits at the discretion of the investigator). All participants were followed up at 1, 6 and 12 months and every 6 months thereafter until the study closed.

A total of 441 participants were randomised (221 to the ECG monitoring group and 220 to the standard monitoring group) and included in the intention-to-treat analyses. During the first 6 months of follow-up, 65 patients in the standard monitoring group had conventional ECG monitoring, 17 patients had 24-hour Holter ECG monitoring, and 1 patient had ECG monitoring with an event recorder.

Continuous ECG monitoring detected more people with atrial fibrillation (19 people, 8.9%) than did standard monitoring (3 people, 1.4%) in the first 6 months of follow-up (hazard ratio=6.4, 95% CI 1.9 to 21.7, $p<0.0001$). By 12 months, people in the continuous ECG monitoring group were more likely to be on anticoagulation therapy (14.7% versus 6.0% in the standard monitoring group) and less likely to have experienced an ischaemic stroke or TIA (7.1% versus 9.1%).

Limitations of these studies include that neither was able to make a causal association between atrial fibrillation and the index stroke or TIA. In addition, randomisation occurred more than a month after the index stroke or TIA in both studies, and neither could record all instances of atrial fibrillation owing to the memory size of the ECG monitoring devices.

Commentary: "These studies clearly show that we need to look harder and look longer for underlying atrial fibrillation in patients presenting with stroke, before labelling someone as having 'cryptogenic stroke'. The diagnosis of 'cryptogenic stroke' is really a diagnosis of exclusion, after very strenuous efforts to exclude atrial fibrillation. Many patients with paroxysmal atrial fibrillation are asymptomatic, and relying on symptoms alone is inadequate for diagnosis.

"A stroke confers the highest risk of a subsequent stroke, and if atrial fibrillation is detected, effective stroke prevention is needed. Prevention essentially comprises oral anticoagulation therapy, whether given as a vitamin K antagonist (VKA; for example, warfarin) with good quality anticoagulation control (average time in therapeutic range >65%), or a non-VKA oral anticoagulant.

"More prolonged atrial fibrillation monitoring improves the detection rate. As part of the standard work-up, 2–4 week ECG monitoring or, where there is a high index of suspicion, an implanted monitoring device, should be considered. This would improve diagnosis of atrial fibrillation, and, by using thromboprophylaxis with oral anticoagulantion, reduce the risks of a subsequent stroke that may be fatal or disabling." *– Professor Gregory Y H Lip, Professor of Cardiovascular Medicine, University of Birmingham, and Aalborg University, Denmark*

Study sponsorship: Gladstone et al. (2014) was funded by the Canadian Stroke Network and Sanna et al. (2014) was funded by Medtronic.

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