Silent cerebral infarctions in atrial fibrillation

A meta-analysis found that the risk of silent cerebral infarctions in people with atrial fibrillation was more than double that in people who did not have atrial fibrillation.

Overview: Atrial fibrillation is a heart condition that causes an irregular and often abnormally fast heart rate. People with atrial fibrillation are at increased risk of stroke (Wolf et al. 1991). People with atrial fibrillation are also at increased risk of cognitive impairment, even if they have not had a symptomatic stroke (Kalantarian et al. 2013). A possible mechanism for this association is that people with atrial fibrillation may be more likely to experience silent cerebral infarctions (Das et al. 2008).

A silent cerebral infarction is a brain lesion caused by a vascular occlusion, which is often found incidentally by MRI or CT in otherwise healthy people or during autopsy (Lee et al. 2000). The prevalence of MRI-diagnosed silent cerebral infarctions in healthy elderly people is 20% (Vermeer et al. 2007). Silent cerebral infarctions may be precursors of symptomatic stroke and cause progressive brain damage that may be associated with vascular dementia.

Current advice: The NICE clinical guideline on atrial fibrillation recommends using the CHA₂DS₂-VASc stroke risk score to assess the risk of stroke in people with atrial fibrillation who have any of the following characteristics:

- symptomatic or asymptomatic paroxysmal, persistent or permanent atrial fibrillation
- atrial flutter
- a continuing risk of arrhythmia recurrence after cardioversion back to sinus rhythm.

The CHA₂DS₂-VASc score uses a number of risk factors – including history of stroke, transient ischaemic attack or thromboembolism – to estimate the risk of stroke in people with atrial fibrillation. Anticoagulation treatment with apixaban, dabigatran etexilate, rivaroxaban or a vitamin K antagonist should be considered in men with a CHA₂DS₂-VASc score of 1 and men or women with a CHA₂DS₂-VASc score of 2 or above.

The NICE pathway on atrial fibrillation brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.
**New evidence:** A meta-analysis by [Kalantarian et al. (2014)](https://doi.org/10.1093/eurheartj/ehu181) investigated the risk of silent cerebral infarctions in people with atrial fibrillation who had not experienced a stroke.

The authors identified observational studies of the association between atrial fibrillation and silent cerebral infarctions in people who had no history of acute or symptomatic stroke. Silent cerebral infarctions were defined as evidence of brain infarctions on imaging or autopsy with no attributable clinical symptoms (such as neurological deficits).

A total of 17 studies (n=7773) from 7 countries were identified, 3 of which were prospective. Silent cerebral infarctions were identified by CT in 6 studies, MRI in 9 studies, and autopsy in 2 studies. The pooled prevalence of silent cerebral infarctions in people with atrial fibrillation was 40% (95% confidence interval [CI] 29% to 51%) in those who underwent MRI and 22% (95% CI 13% to 32%) in those who had CT.

Analysis of the association between atrial fibrillation and silent cerebral infarctions was restricted to 9 studies (n=4407) that used imaging for diagnosis and reported risk estimates. Overall, 230 (46%) people with atrial fibrillation and 610 (16%) people without atrial fibrillation had silent cerebral infarctions. The risk of silent cerebral infarctions was twice as high in people with atrial fibrillation compared with those who did not have atrial fibrillation among people with no history of symptomatic stroke (odds ratio=2.62, 95% CI 1.81 to 3.80).

Limitations of this analysis included that many of the studies were retrospective and cross-sectional, and the studies were of variable quality. Autopsy studies were heterogeneous and low quality, so were excluded from the meta-analysis. Information on the anticoagulation status of participants was not available for many studies, and the prevalence of silent cerebral infarctions diagnosed by MRI varied depending on the diagnostic criteria used.

**Commentary by Professor Jonathan Mant, Professor of Primary Care Research, Primary Care Unit, University of Cambridge:**

“This study adds to the body of research that suggests that atrial fibrillation is associated with increased risk of cognitive impairment and dementia, by providing evidence of the likely mechanism through which it might do this — that is, by increasing risk of silent cerebral infarction.

“A mainstay of treatment of atrial fibrillation is to reduce risk of stroke through anticoagulation. Currently, anticoagulation is offered on the basis of an assessment of the risk of clinical stroke in atrial fibrillation using the CHA\textsubscript{2}-DS\textsubscript{2}-VASc score. This study raises the question as to whether risk of silent cerebral infarction also needs to be taken into account in decisions concerning anticoagulation.

“However, there are two questions that need to be answered before any changes to current practice are considered. Firstly, does anticoagulation reduce risk of silent cerebral infarction, and risk of cognitive impairment and dementia? If this was the case, the risk:benefit ratio and indeed the cost effectiveness of anticoagulation could change, so that anticoagulation might become indicated for people with atrial fibrillation who are at lower risk of stroke. Secondly, does presence of silent cerebral infarction increase risk of subsequent clinical stroke? If this was the case, then some refinement of the CHA\textsubscript{2}-DS\textsubscript{2}-VASc score might be necessary.

“Unfortunately, there are no randomised trials or clear-cut evidence from observational studies to answer either of these questions. Pending such research, this meta-analysis raises our awareness of the potential invisible impact of atrial fibrillation over and above the recognised overt clinical manifestations.”

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