Anticoagulants Versus Antiplatelet Therapy for Preventing Stroke in Patients With Nonrheumatic Atrial Fibrillation and a History of Stroke or Transient Ischemic Attack

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People with nonrheumatic atrial fibrillation (NRAF) who have had a transient ischemic attack (TIA) or a minor ischemic stroke are at high-risk of recurrent stroke. Both warfarin and aspirin have been shown to reduce the recurrence of vascular events.

Objectives
The objective of this review was to compare the effect of anticoagulants with antiplatelet agents, for secondary prevention, after a stroke or TIA, in patients with NRAF.

Search Strategy
This review has drawn on the search strategy developed for the Stroke Group as a whole. Relevant trials were identified in the Stroke Group Trials Register (last search June 9, 2003). We also contacted researchers in the field to identify further published and unpublished studies.

Selection Criteria
Randomized trials comparing oral anticoagulants with antiplatelet agents in patients with NRAF and a previous TIA or minor ischemic stroke.

Data Collection and Analysis
Both reviewers assessed trial quality and extracted data. The main outcomes considered were (1) fatal or nonfatal recurrent stroke; (2) all major vascular events: vascular death (including fatal bleeds), recurrent stroke (both ischemic and hemorrhagic), myocardial infarction, and systemic embolism; (3) any intracranial bleed; (4) major extracranial bleed.

Results
Two trials were identified. In the European Atrial Fibrillation Trial (EAFT) 455 patients received either anticoagulants (International Normalized Ratio [INR] 2.5 to 4.0), or aspirin (300 mg/d). Patients joined the trial within three months of transient ischemic attack or minor stroke. The mean follow up was 2.3 years. In the Studio Italiano Fibrillazione Atriale (SIFA) trial, 916 patients with NRAF and a TIA or minor stroke within the previous 15 days were randomized to open label anticoagulants (INR 2.0 to 3.5) or indobufen (a reversible platelet cyclooxygenase inhibitor, 100 or 200 mg BID). The follow-up period was one year. The combined results show that anticoagulants were significantly more effective than antiplatelet therapy both for the prevention of all vascular events (Peto odds ratio [Peto OR] 0.67; 95% confidence interval [CI], 0.50 to 0.91) and for recurrent stroke (Peto OR 0.49; 95% CI, 0.33 to 0.72). Major extracranial bleeding complications occurred more often in patients on anticoagulants (Peto OR 5.16; 95% CI, 2.08 to 12.83), but the absolute difference was small (2.8% per year versus 0.9% per year in EAFT and 0.9% per year versus 0% in SIFA). Warfarin did not cause a significant increase of intracranial bleeds.

Implications for Practice
In patients with NRAF and a recent nondisabling stroke or TIA, oral anticoagulants were more effective than antiplatelet agents for preventing recurrent stroke and major vascular events. However, anticoagulants were associated with a significant increase in the risk of major extracranial bleeds. These data support the routine use of oral anticoagulants in patients with NRAF and a recent nondisabling stroke or TIA.

Implications for Research
The excess of major extracranial bleeds with warfarin highlights the need to identify safer anticoagulant regimens or new agents of comparable efficacy but greater safety. Similarly, there is a need to identify more effective antiplatelet...
agents for use in NRAF patients who have a contraindication to oral anticoagulants.

**Conclusions**

The evidence from 2 trials suggests that anticoagulant therapy is superior to antiplatelet therapy for the prevention of stroke in people with NRAF and recent nondisabling stroke or TIA. The risk of extracranial bleeding was higher with anticoagulant therapy than with antiplatelet therapy.

Note: The full text of this review is available in the Cochrane Library (for subscribers: http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME). The full article should be cited as: Saxena R, Koudstaal PJ. Anticoagulants versus antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attack (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2004. Chichester, UK: John Wiley & Sons, Ltd.

**Key Words:** anticoagulants ■ atrial fibrillation ■ platelet aggregation inhibitors ■ stroke prevention
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