Review: Antithrombotic agents prevent stroke in nonvalvular atrial fibrillation


**Question**
How efficacious and safe are anticoagulants and antiplatelet agents for preventing stroke in patients with nonvalvular atrial fibrillation (AF)?

**Data Sources**
Randomized controlled trials were identified by searching MEDLINE (1966 to 1999), making contact with the Cochrane Collaboration Stroke Review Group and Antithrombotic Trialists Collaboration, and contacting experts.

**Study Selection**
Trials were included if they evaluated long-term (> 3 mo) use of antithrombotic agents in patients with nonvalvular AF. The exclusion criterion was AF associated with prothetic cardiac valves or mitral stenosis.

**Data Extraction**
Data were extracted on patient numbers, follow-up duration, agents studied, type of prevention (primary or secondary), and outcomes (all-cause mortality, stroke, ischemic stroke, intracranial hemorrhage, and major extracranial hemorrhage).

**Main Results**
16 trials (9874 patients) met the inclusion criteria. 10 studies evaluated warfarin. On average, the 1-year risk for stroke in the placebo group was approximately 5% in the primary prevention studies and 12% in the secondary prevention studies. All agents were more effective than placebo at reducing the incidence of stroke: adjusted-dose warfarin (6 trials, 2900 patients, relative risk reduction [RRR] 62%, 95% CI 48% to 72%), aspirin (6 trials, 3119 patients, dose range 50 to 1300 mg/d, RRR 22%, CI 2% to 38%), and all antiplatelet agents (6 trials, 3337 patients, most of whom were taking aspirin; RRR 24%; CI 7% to 39%). Adjusted-dose warfarin was more effective than aspirin for reducing stroke (RRR 36%, CI 14% to 52%). Warfarin was associated with more intracranial (0.3% vs 0.1%/y) and major extracranial hemorrhages than placebo (0.6%/y vs 0.3%/y). Similar increases in the rate of hemorrhage were seen when warfarin was compared with aspirin but not when aspirin was compared with placebo. Comparisons of other agents (10 studies) show few outcome events or adverse effects and inconclusive results. The absolute benefit of each intervention depends on the baseline risk of certain groups (e.g., primary vs secondary prevention, individual patients). Estimates of the number needed to treat (NNT) to prevent 1 additional stroke at 1 year for warfarin compared with placebo were 37 for primary prevention and 12 for secondary prevention. For aspirin compared with placebo, estimated NNTs were 67 for primary prevention and 40 for secondary prevention; for warfarin compared with aspirin, estimated NNTs were between 42 and 250 for primary prevention, depending on the underlying risk for stroke, and 21 for secondary prevention.

**Conclusions**
Antithrombotic agents are more effective at preventing stroke in patients with atrial fibrillation than is placebo. Warfarin is more effective than aspirin. The balance of benefit and risk between warfarin and aspirin depends on the underlying risk for stroke and hemorrhage in each patient.

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For correspondence: Dr. R.G. Hart, Department of Medicine (Neurology), University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284, USA. FAX 210-567-4659.

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**References**