

# Review: Warfarin prevents stroke in nonrheumatic atrial fibrillation but has a higher risk for hemorrhage than other agents

Segal JB, McNamara RL, Miller MR, et al. **Anticoagulants or antiplatelet therapy for non-rheumatic atrial fibrillation and flutter.** *Cochrane Database Syst Rev.* 2001;(1):CD001938 (latest version 29 Nov 2000).

## QUESTION

In patients with nonrheumatic atrial fibrillation (AF), how effective are anticoagulants and antiplatelet drugs in preventing thromboembolic complications?

## DATA SOURCES

Studies were identified by searching 3 databases and relevant journals.

## STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) evaluating warfarin, aspirin, combined low-dose warfarin and aspirin, low-molecular-weight heparin, or indobufen for prevention of thromboembolism in AF or atrial flutter and if the outcomes were stroke, major bleeding, or death.

## DATA EXTRACTION

Data were extracted on study quality; patient characteristics; therapeutic protocol, including intensity of coagulation and percentage of time inside and outside of the target range.

## MAIN RESULTS

14 RCTs were included. 6 RCTs compared warfarin with placebo: Warfarin reduced the risk for stroke but increased the risk for major hemorrhage; the 23% relative reduction in total mortality was not statistically significant. 4 RCTs compared aspirin with placebo: The modest reduction in stroke (16%) was not significant; no difference was seen for

hemorrhage or mortality. 5 RCTs compared warfarin with all antiplatelet drugs: Warfarin reduced the risk for stroke and showed no difference for hemorrhage or mortality. 4 RCTs compared warfarin with aspirin: A moderate decrease for stroke was shown with warfarin, and no difference was shown for hemorrhage or mortality. The results for stroke and hemorrhage are in the Table. Adjusted-dose warfarin reduced stroke more than did low-dose warfarin plus aspirin (2 RCTs). No differences were seen in comparisons of warfarin and indobufen (1 RCT) or

low-molecular-weight heparin and placebo (1 RCT).

## CONCLUSIONS

In patients with nonrheumatic atrial fibrillation, warfarin prevents stroke among those with average or higher risk and is more effective than antiplatelet drugs. The risk for major hemorrhage is increased with warfarin.

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### Anticoagulants or antiplatelets (APs) to prevent stroke in nonrheumatic atrial fibrillation and flutter\*

Outcomes†	Comparison	Weighted event rates	RRR (95% CI)	NNT (CI)
Stroke	Warfarin vs placebo	2.9% vs 8.7%	66% (52 to 76)	18 (14 to 25)
	Aspirin vs placebo‡	9.1% vs 11.2%	16% (-28 to 45)	Not significant
	Warfarin vs APs	3.2% vs 5.0%	36% (10 to 54)	56 (33 to 250)
	Warfarin vs aspirin	3.6% vs 5.4%	33% (3 to 54)	56 (29 to 500)
			<b>RRI (CI)</b>	<b>NNH (CI)</b>
Hemorrhage	Warfarin vs placebo	2.2% vs 0.9%	139% (27 to 348)	77 (46 to 250)
				<b>RRR (CI)</b>
	Aspirin vs placebo	1.3% vs 1.4%	5% (-81 to 51)	Not significant
			<b>RRI (CI)</b>	<b>NNH</b>
	Warfarin vs APs	1.5% vs 0.8%	83% (-6 to 258)	Not significant
	Warfarin vs aspirin	1.6% vs 1.0%	56% (-24 to 221)	Not significant

\*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

†Duration of follow-up not reported.

‡Random-effects model was used.

## COMMENTARY

Despite convincing evidence that warfarin therapy is highly effective in preventing stroke in patients with chronic AF, only one half of eligible patients are receiving this treatment (1). The most commonly cited reasons for warfarin underuse are concerns about bleeding in elderly patients and the feasibility of anticoagulation monitoring (2).

For clinicians who remain unsure about the risk-benefit ratio of warfarin therapy in patients with chronic AF, the meta-analysis by Segal and colleagues provides a concise balance sheet of potential benefits and harms associated with warfarin and aspirin therapy. For warfarin therapy, 18 patients need to be treated to prevent 1 additional stroke (RRR 66%), whereas 1 additional major bleed will occur after the treatment of 77 patients. This risk-benefit ratio is acceptable because about 70% of cardioembolic strokes are fatal or are associated with major disability (3). About 5% of warfarin-associated bleeds are intracranial, and most other bleeds are not associated with long-term morbidity (4). Aspirin therapy is not associated with an increased risk for bleeding, but it has questionable efficacy in overall stroke prevention (RRR 16%), and its benefit may be limited to the prevention of thrombotic stroke.

Another consideration in deciding about treatment options is a patient's risk profile. Patients with previous stroke, left ventricular dysfunction, age > 75 years, or hypertension are at high risk for stroke, whereas those with diabetes, coronary artery disease, or age 65 to 75 years are at moderate risk, and those < 65 years with no risk factors are at low risk. Patients > 75 years of age are at highest risk for bleeding, but will benefit most from warfarin therapy.

In summary, warfarin should be considered in all patients with chronic AF, and aspirin should be used only in patients with a contraindication to warfarin, or those at low risk for stroke.

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## References

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