

Review: Anticoagulants may be better than antiplatelet agents for nonfatal stroke but not other vascular or fatal events in nonrheumatic AF

Our systematic review of randomized controlled trials of direct head-to-head comparisons of adjusted-dose warfarin with antiplatelet drugs, abstracted in this issue (1), showed no significant benefit for vascular deaths (odds ratio [OR] 0.86, 95% CI 0.63 to 1.17) or combined fatal and nonfatal vascular events (OR 0.79, CI 0.61 to 1.02). Our review also highlighted the problems of the Atrial Fibrillation, Aspirin, and Anticoagulation Study (AFASAK)-1 trial of inadequate concealment of randomization, nonblinded assessment of outcomes, and high losses to follow-up (2). This trial showed the largest benefit and was the only trial with a significant effect for its primary trial-defined outcome.

Comparison of fatal events provides the most robust evidence of whether anticoagulation is better than aspirin because biased ascertainment is less likely. Meta-analysis provides more adequate power to assess less common, but more certain, fatal outcomes. We feel practitioners would be misguided to base treatment decisions on a marginally significant finding for 1 outcome—nonfatal stroke—which tends to be overemphasized. Use of anticoagulation is consistent with both major treatment benefit and with modest harm in terms of vascular events. Clearly, more evidence is needed to guide clinical practice.

Anticoagulants may be more effective than antiplatelet drugs in secondary prevention. Surprisingly, the primary publication of the European Atrial Fibrillation Trial (EAFT) (3) did not present data allowing direct comparison of patients randomly allocated to aspirin and warfarin; this resulted in its exclusion from our review. Combined fixed low-dose warfarin with aspirin, evaluated in the Stroke Prevention in Atrial Fibrillation (SPAF)-III trial (4), is seldom used clinically and is not relevant to the question of whether adjusted-dose anticoagulation is superior to antiplatelet drugs because a direct head-to-head comparison was not made. Vascular deaths did not differ between the 2 treatment groups.

None of the trials considered the costs of a policy of using anticoagulation, which is at least 15 times more expensive than using aspirin (5). Taking patient preferences into account is essential given the risks associated with anticoagulation, the lifelong nature of the treatment, and doubt about its true benefits. A study that assessed patient preferences in formal decision analysis concluded that “taking account of patients’ preferences would lead to fewer prescriptions for warfarin than under published guideline recommendations” (6). However, a recent Canadian report suggests that patients are, on the average, willing to accept the risk for bleeding in exchange for a reduced risk for a stroke (7). More work examining the determinants of patient preferences and the cost-effectiveness of adjusted-dose warfarin is needed to resolve current uncertainties.

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References

1. ACP J Club. 2001 Sep-Oct;135:60. Abstract of: Taylor FC, Cohen H, Ebrahim S. *BMJ*. 2001;322:321-6.

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3. European Atrial Fibrillation Study Group. *Lancet*. 1993;342:1255-62.
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6. Protheroe J, Fahey T, Montgomery AA, Peters TJ. *BMJ*. 2000;320:1380-4.
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In response:

Ebrahim and Taylor are correct to suggest that clinicians should consider all vascular events when deciding whether to treat patients who have atrial fibrillation with oral anticoagulants rather than aspirin. However, they are wrong to downplay the importance of nonfatal stroke. Patients rightly fear a disabling stroke, and anticoagulation is given to patients with atrial fibrillation primarily to decrease their risk for stroke.

In my opinion, the rationale for excluding the EAFT and SPAF-III studies (both of which studied patients with atrial fibrillation who were at high risk for stroke) is unconvincing. The EAFT authors could have been approached for the data required for the systematic review. As for SPAF-III, I agree that low-dose warfarin plus aspirin is rarely used clinically (a good thing, too—it was much less effective than full-dose warfarin!). However, to argue that SPAF-III should not be included in the systematic review because low-dose warfarin was also used in the aspirin-treated group (which would, if anything, increase the apparent efficacy of the aspirin-containing treatment) strikes me as a triumph of methodologic rigor over clinical common sense. At the very least, a sensitivity analysis with and without SPAF-III should have been done. With the addition of these 2 trials, AFASAK-1 would no longer be an outlier.

Finally, it is important to remember that the risk for stroke in patients with atrial fibrillation varies markedly depending on comorbid conditions, which should be taken into account when deciding whether to recommend warfarin or aspirin (1).

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1. Glasziou P, Guyatt GH, Dans AL, et al. *ACP J Club*. 1998 Nov-Dec;129:A-15-16. Evidence-Based Medicine. 1998 Nov-Dec;3:165-6.

Correction

The Bayes nomogram that appeared in the glossary of *ACP Journal Club* in the September/October and November/December 1999 issues should not be used because it contains 2 errors:

1. The likelihood ratio scale is imperfectly drawn, giving inaccurate readings in parts of the nomogram.
2. The lower 500 on the likelihood ratio scale should be 200.

A correct version of the nomogram can be viewed on Best Evidence.