

## FPIN's Clinical Inquiries

### Which Patients with Atrial Fibrillation Do Not Need Anticoagulation Therapy with Warfarin?

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group ([http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)).

This series of Clinical Inquiries is coordinated for American Family Physician by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN. If you are interested in submitting questions to be answered or writing answers for this series, go to <http://www.fpin.org> or contact [CI2Editor@fpin.org](mailto:CI2Editor@fpin.org).

## Searchable Question

Which patients with atrial fibrillation do not need anticoagulation therapy with warfarin?

## Evidence-Based Answer

Anticoagulation therapy with warfarin is not indicated for use in patients with non-valvular atrial fibrillation who are at low risk for embolic cerebral vascular events. The classification of "low risk for embolic stroke" is defined as a 1 percent annual risk for stroke or lone atrial fibrillation (i.e., age younger than 65 years without history of hypertension, transient ischemic attack, stroke, coronary heart disease, recent congestive heart failure, or diabetes).

Anticoagulation therapy with warfarin is beneficial in patients with atrial fibrillation who are at moderate or high risk for stroke. Patients with absolute contraindications to anticoagulation therapy (e.g., thrombocytopenia, recent trauma or surgery, hemorrhagic stroke, alcoholism) should not take warfarin.<sup>1,2</sup> [Strength of recommendation: A, based on meta-analyses of large randomized controlled trials (RCTs)]

## Evidence Summary

A number of meta-analyses of RCTs evaluating prevention of stroke in patients with atrial fibrillation demonstrated the benefits of warfarin therapy.<sup>1,2</sup> The Atrial Fibrillation Investigators pooled data from five large RCTs covering 3,691 patient-years. The annual rate of stroke was found to be 4.5 percent among the control groups and 1.4 percent in the warfarin groups. The

absolute risk reduction (RR) was 3.1 percent (95 percent confidence interval [CI], 2.3 to 3.6 percent), and the number needed to treat (NNT) was 32.<sup>1</sup>

A 1999 meta-analysis of 16 RCTs covering 16,785 patient-years showed that the placebo groups had a 6 percent annual stroke rate compared with a 2.2 percent annual stroke rate in the warfarin groups. The absolute RR was 3.8 percent (95 percent CI, 2.9 to 4.3 percent), and the NNT was 26.<sup>2</sup>

Both meta-analyses reported slightly higher annual rates of major bleeding events among patients taking warfarin (1.3 percent) compared with those taking placebo (1 percent) or aspirin (1 percent).<sup>1,2</sup>

The meta-analyses showed aspirin therapy had a modest stroke risk reduction compared with placebo. In the first meta-analysis, the absolute RR was 1.6 percent (95 percent CI, 0.2 to 2.6 percent), and the NNT was 62.1. In the second meta-analysis, the absolute RR was 1.7 percent (95 percent CI, 0.2 to 3.0 percent), and the NNT was 59.<sup>2</sup>

Risk stratification and subgroup analysis of data from the Atrial Fibrillation Investigators showed that warfarin therapy has limited benefit in patients who have atrial fibrillation and no other risk factors. Patients younger than 65 years without other risk factors had an annual risk for stroke of 1 percent whether they were taking warfarin or not. In patients with higher risk for embolic cerebral vascular accidents, the relative RR remained constant, and the absolute RR increased with the annual stroke rate. Stroke risk was reduced from an untreated rate ranging from 4.3 to 12 percent annually to a treated rate of 1.1 to 4 percent annually.<sup>3</sup>

Patients with absolute contraindications to warfarin anticoagulation therapy (e.g., thrombocytopenia, recent trauma or surgery, hemorrhagic stroke, alcoholism) should not receive warfarin. These patients were systematically excluded from all RCTs of warfarin and atrial fibrillation.

Based on this evidence, warfarin therapy is not indicated for low-risk patients but is beneficial in moderate- and high-risk patients. Defining the exact risk for stroke is the critical task in determining if a patient should take warfarin (see accompanying table).<sup>4-7</sup> As the risk for stroke increases, the NNT decreases. A relatively small but statistically significant risk for hemorrhage with warfarin therapy requires that individual patient characteristics be considered.

Definitions of Low Risk for Stroke\*

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Model	Definition
Joint Panel of the American Academy of Family Physicians and the American College of Physicians <sup>4</sup>	History or presence of no more than one of the following: <ul style="list-style-type: none"><li>• CHF within 100 days</li><li>• Hypertension</li><li>• Age &gt; 75 years</li><li>• Diabetes</li></ul>
American College of Chest Physicians <sup>5</sup>	Age < 65 years and all of the following: <ul style="list-style-type: none"><li>• No hypertension</li><li>• No diabetes</li><li>• No CHD</li><li>• No CHF</li></ul>
American College of Cardiology, American Heart Association, and European Society of Cardiology <sup>6</sup>	Age < 60 years, CHD but no CHF (LVEF > 0.35) and no hypertension
	<i>or</i>
Stroke Prevention in Atrial Fibrillation III Study <sup>7</sup>	Age < 75 years, but no CHF, hypertension, CHD, or diabetes Male or female, age < 75 years, and all of the following: <ul style="list-style-type: none"><li>• No hypertension</li><li>• No recent CHF</li><li>• No severe LV dysfunction</li></ul>

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\*-All models consider a history of thromboembolism to be high risk.

CHF = congestive heart failure; CHD = coronary heart disease; LVEF = left ventricular ejection fraction; LV = left ventricle.

Information from references 4 through 7.

## Recommendations from Others

The American Academy of Family Physicians, the American College of Physicians,<sup>4</sup> the American College of Chest Physicians,<sup>5</sup> the American College of Cardiology, the American Heart Association, and the European Society of Cardiology<sup>6</sup> have published recommendations consistent with this evidence-based answer.

## Clinical Commentary

In practice, the decision to anticoagulate with warfarin can be complex. The evidence supports quantifying the patient's risk for embolic stroke. However, patients at greatest risk for stroke often have a risk for hemorrhage or difficulty complying with warfarin therapy monitoring. In some patients, other antiplatelet and antithrombotic agents such as aspirin and clopidogrel (Plavix) remain a reasonable alternative.

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