

## PRACTICE PARAMETER STROKE PREVENTION IN PATIENTS WITH NONVALVULAR ATRIAL FIBRILLATION

Report of the Quality Standards Subcommittee of the American Academy of Neurology

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Nonvalvular atrial fibrillation (AF) is present in about 1.8 million people in the United States<sup>1</sup> and in 16% of patients with an ischemic stroke.<sup>2</sup> The incidence of both AF and stroke increases with age, so that AF is present in over one-third of individuals older than 75 years,<sup>2</sup> although the proportion may be less in African Americans and Hispanics.<sup>3</sup> About one-third of patients with AF are unaware of their condition.<sup>4</sup> Treatments of proven efficacy are available that reduce the risk of ischemic stroke in patients with AF. Because ischemic stroke is common and produces substantial disability, therapies that can reduce the risk of stroke are worthy of consideration by neurologists and, when appropriate, should be implemented.

The mechanism of most ischemic strokes in patients with AF is probably cardioembolic.<sup>5</sup> However, causes other than cardioembolism may play a role in about 30% of strokes in patients with AF.<sup>5</sup> Small, deep infarcts are relatively uncommon in patients with AF.<sup>5,6</sup> Because chronic anticoagulation is already the accepted standard of practice to reduce risk of thromboembolism in patients with AF for whom a condition that causes major perturbation of blood flow is known to be present (e.g., mitral stenosis, prosthetic mitral valve), stroke prevention in these patients is not addressed in this practice parameter. Rather, evidence supporting available treatments to prevent stroke in patients with nonvalvular AF is reviewed and the strength of the evidence is evaluated.

**Justification.** The annual rate of stroke among patients with AF is about 5% per year, and one in three people with nonvalvular AF will suffer stroke if untreated.<sup>7</sup> Risk of stroke is even higher in a patient with AF if hypertension, prior stroke, TIA, or left ventricular systolic dysfunction is also present.<sup>7-9</sup> The cost of therapy that can prevent stroke in patients with AF is modest compared with the cost of rehabilitation, lost income, and deterioration in quality of life that most strokes produce. Some 75,000 strokes per year occur in Americans with AF, and it is timely for the Quality Standards Subcommittee (QSS) of the American Academy of Neurology (AAN) to make recommendations for stroke prevention in patients with AF. The background paper on which this practice parameter was based may be consulted for more details.<sup>10</sup>

**Method.** Literature in English published between 1991 and 1997 was searched using PLUSNET with key words of atrial fibrillation with stroke, embolism, or thromboembolism. From these sources, the parameter focused on randomized clinical trials,<sup>7,9,11-13</sup> key case-control studies,<sup>14,15</sup> and a large cohort study.<sup>16</sup>

**Strength of evidence.** Stratification of AF patients by the presence of additional risk factors for stroke helps select those who are at highest risk and maximizes the potential benefit of warfarin (table).

Class I: Adjusted-dose warfarin reduces risk of stroke in patients with AF by about 70%. Warfarin is safe for patients who can be carefully monitored, preferably with the international normalized ratio (INR) or, if the INR is unavailable, with prothrombin time (PT).

Aspirin reduces risk of stroke in patients with AF by about 20%, and thus is less efficacious than warfarin.

Class II: No relevant articles pertaining to the recommendations were found.

Class III: In elderly patients (over age 75 years) with AF, warfarin may be used with a lower INR target of 2.0 (target range 1.6 to 2.5) to decrease risk of hemorrhage. However, some authorities disregard age and accept a higher INR target of 2.5 (target range 2.0 to 3.0) as appropriate and safe.

In patients in whom warfarin is contraindicated, aspirin is an alternative for reducing risk of stroke in patients with AF, although aspirin is less efficacious.

**Recommendations.** *Standard.* Patients with AF should be considered for anticoagulation because of its clear efficacy in stroke prevention and its low risk of bleeding when INR is appropriately monitored.

**Guidelines.** For patients with atrial fibrillation aged 75 or younger who are at high risk of stroke (see table) and are deemed safe candidates for anticoagulation, treatment with warfarin and a target INR of 2.5 (range 2.0 to 3.0) is recommended.

**Options.** For those over age 75 years, a lower INR target of 2.0 (range 1.6 to 2.5) may be acceptable to minimize risk of bleeding. However, because this lower intensity anticoagulation has not been separately established as adequately efficacious for high-risk patients with AF, a higher target INR of 2.5 (range 2.0 to 3.0) is recommended for such patients regardless of age as an alternative.

For patients with AF deemed unable to receive anticoagulants or those deemed to be at low risk of stroke (see table), aspirin (325 mg/day) is recommended. However, aspirin has not been established as efficacious for these specific subgroups of patients with atrial fibrillation by clinical trials.

For patients with AF considered to have a moderate risk of stroke, the choice of warfarin or aspirin should particularly consider the individual patient's bleeding risk during anticoagulation and patient preferences.

**Table** Risk stratification schemes for patients with nonvalvular atrial fibrillation

Scheme	High-risk	Moderate-risk	Low-risk
AFI/ACCP Consensus <sup>7</sup>			
Criteria	History of hypertension Diabetes Prior stroke or TIA Coronary artery disease Congestive heart failure	Age $\geq$ 65 y, no high-risk features	Age < 65 y, no high-risk features
Stroke risk, no therapy	$\approx$ 6%/y	$\approx$ 2%/y*	$\approx$ 1%/y
SPAF III Study <sup>8,16</sup>			
Criteria	Systolic BP > 160 mm Hg Left ventricular dysfunction <sup>†</sup> Prior stroke or TIA Women > 75 y	History of hypertension, no high-risk features	No high-risk features or history of hypertension
Stroke risk with aspirin	$\approx$ 8%/y <sup>‡</sup>	$\approx$ 3.5%/y	$\approx$ 1%/y

\* In the AFI/ACCP Consensus conference scheme, the ischemic stroke rate in those without high-risk features was 1.6%/y in the age group 60-69 y, 2.1% in those 70-79 y, and 3.0%/y in those over age 80 y.<sup>7</sup>

<sup>†</sup> Impaired left ventricular function included recent congestive heart failure or fractional shortening  $\leq$ 25% by M-mode echocardiography.

<sup>‡</sup> For those without prior stroke/TIA, the estimated event rate was  $\approx$ 6%/y; for those with prior stroke/TIA it was nearly 12%/y; those with multiple risk factors have even higher stroke rates.

SPAF = Stroke Prevention in Atrial Fibrillation Study; AFI = Atrial Fibrillation Investigators; ACCP = American College of Chest Physicians; CI = confidence intervals; Hx = history; TIA = transient ischemic attack; AF = atrial fibrillation.

**Future research.** A key issue is the reliable stratification of stroke risk to identify AF patients at high versus low risk of ischemic stroke. The generalizability of current risk stratification schemes based on clinical trials (see table) to clinical practice warrants further study.

The optimal intensity of anticoagulation for subgroups of AF patients (e.g., very elderly or those with prior stroke) and better quantitative definition of contraindications to anticoagulation merit further investigation to permit safer, more efficacious anticoagulation.

The effects of cardioversion and pharmacologic efforts to maintain sinus rhythm on stroke risk and quality of life remain to be determined.

Patient preference for use of aspirin versus warfarin (and required monitoring as well as increased cost of the latter) must be taken into account in selecting appropriate therapy for stroke prevention.

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**Note.** This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

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## Appendix 1

### Definitions for classification of evidence

Class I: Evidence provided by one or more well-designed randomized controlled clinical trials, including overviews (meta-analyses) of such trials.

Class II: Evidence provided by well designed observational studies with concurrent controls (e.g., case control and cohort studies).

Class III: Evidence provided by expert opinion, case series, case reports, and studies with historical controls.

### Definitions for strength of recommendations

Standard: A principle for patient management that reflects a high degree of clinical certainty (usually this requires class I evidence that directly addresses the clinical question, or overwhelming class II evidence when circumstances preclude randomized clinical trials).

Guideline: A recommendation for patient management that reflects moderate clinical certainty (usually this requires class II evidence or a strong consensus of class III evidence).

Practice option: A strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).

Practice advisory: A practice recommendation for emerging and/or newly approved therapies or technologies based on evidence from at least one class I study. The evidence may demonstrate only a modest statistical effect or limited (partial) clinical response, or significant cost-benefit questions may exist. Substantial (or potential) disagreement among practitioners or between payers and practitioners may exist.

## Appendix 2

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