

**ATHENS CARDIOLOGY UPDATE 2008**

# Similar Incidence of Stroke in Paroxysmal Versus Sustained Atrial Fibrillation?/ Performance Measures for Atrial Fibrillation

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**KEY WORDS:** *atrial fibrillation;  
atrial flutter; thromboembolic stroke;  
performance measures*

## ABSTRACT

No clear evidence exists regarding the effect of atrial fibrillation (AF) duration and frequency on the occurrence of stroke. Some studies have suggested a lower stroke risk in paroxysmal than in persistent AF. In contrast, other studies have reported a comparable stroke risk of paroxysmal to permanent AF. Upcoming trials such as the TRENDS and the ASSERT studies will provide further insight into the direct relation of AF duration and systemic embolism in a large group of patients with an implantable device. Recently, an ACC/AHA physician consortium provided clinical performance measures for adults with nonvalvular atrial fibrillation or atrial flutter.

## INTRODUCTION

Atrial fibrillation (AF) remains a challenge to manage. Although there are issues concerning rate and rhythm control, prevention of thromboembolism remains the most important aspect of management. Untreated, strokes will occur in about 2% to 5% of patients per year, and the strokes caused by AF can be quite devastating [1-3]. Anticoagulant therapy with vitamin K antagonists such as warfarin sodium can substantially reduce the risk of AF-related thromboembolism, but at the risk of incurring more hemorrhagic complications [1].

Accurate stratification of patients with AF by thromboembolism risk should ideally target the use of warfarin for patients at highest risk of thromboembolism and reduce the exposure of low-risk patients to the complications of warfarin [4-6].

## PAROXYSMAL VS PERMANENT ATRIAL FIBRILLATION

Several risk stratification models of different complexity have been introduced to identify AF patients who benefit from oral anticoagulation [7]. In none of these models, the type of AF—paroxysmal versus persistent or permanent—has emerged as an independent predictor of thromboembolic events. Thus, the most recent guidelines on AF therapy recommend the use of oral anticoagulation for patients with stroke risk factors irrespective of the type of AF [2]. Paroxysmal AF is a self-terminating arrhythmia, within a short period of time, often less than 24 hours [2].

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A subanalysis of the SPAF (Stroke Prophylaxis in Atrial Fibrillation) trials looked at the risk of stroke in patients having “intermittent” AF in comparison with those having continuous AF [8]. This study in 460 patients with paroxysmal AF found similar incidence of thromboembolic events for both types of AF. However, the definition of intermittent AF was completely different from what we now agree is paroxysmal AF [2]. Furthermore, this analysis was based on the SPAF trials conducted more than 15 years ago and was limited to patients treated with aspirin. Treatment for AF and for the underlying cardiovascular disease has markedly changed, for instance regarding therapy for arterial hypertension or current international normalized ratio (INR) management. Finally, Hart et al. used only data from patients treated with aspirin and not with oral anticoagulation.

The observational Euro Heart Survey on AF (2003–04) enrolled 1509 paroxysmal, 1109 persistent, and 1515 permanent AF patients, according to the 2001 American College of Cardiology, American Heart Association, and the European Society of Cardiology guidelines definitions [9]. A 1-year follow-up was completed. Permanent AF patients had at baseline a worse stroke risk profile than paroxysmal and persistent AF patients. In paroxysmal AF, the risk for stroke, any thromboembolism, major bleeding and the combined endpoint of cardiovascular mortality, any thromboembolism, and major bleeding was comparable in persistent and permanent AF, in both univariable and multivariable analyses.

This observation is consistent with the results reported by Hohnloser et al [10]. The data provided by Hohnloser et al. were derived from the patients enrolled in the ACTIVE W trial (Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events). The ACTIVE W was a trial comparing oral anticoagulation to combined antiplatelet therapy with aspirin and clopidogrel for prevention of vascular events in 6,706 AF patients. The incidence of thromboembolic events and major bleeds were compared in patients with paroxysmal and persistent or permanent AF. The above mentioned data may explain observations made in other contemporary trials such as the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial [11]. In the AFFIRM trial, the prevalence of ischemic stroke was 7.1% in patients in whom rhythm control was attempted, compared with 5.5% in those who were randomized to rate control. It is possible that episodes of (asymptomatic) paroxysmal AF in the rhythm control arm for which patients did not receive anticoagulation therapy may account for this finding.

On the other hand, emerging evidence suggests that brief episodes of self-terminating AF do not constitute the same risk as long-lasting AF [12]. Comparison of stroke rates in the anticoagulation-treated arms of several trials in relation to proportion with paroxysmal AF showed that trials with a higher proportion of patients with paroxysmal AF usually

have a lower risk of stroke [13]. Two large studies examining the relevance of duration of AF (“burden”) to the risk of thromboembolism using device telemetry are currently in progress [14,15].

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## PERFORMANCE MEASURES FOR ATRIAL FIBRILLATION

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The American Heart Association and the American College of Cardiology have jointly issued clinical performance measures for adults with nonvalvular atrial fibrillation (AF) or atrial flutter, which were published concurrently in the Journal of the American College of Cardiology and Circulation [16]. Three performance risk measures were identified: assessment of thromboembolic risk factors, long-term anticoagulation therapy, and monthly INR measurement.

The following are 10 points to remember from this scientific statement.

1. Antithrombotic therapy is indicated for all patients with AF except those with lone AF or contraindications.
2. Assessment of thromboembolic risk factors should include prior stroke/transient ischemic attack (TIA), age  $\geq 75$  years, hypertension, diabetes, and heart failure or left ventricular (LV) systolic dysfunction.
3. Prior stroke/TIA is the strongest risk factor and is an indication for anticoagulation with warfarin.
4. Rheumatic mitral stenosis also is a strong risk factor for stroke and is an indication for warfarin even if no other risk factors are present.
5. Warfarin also is indicated for patients with  $>1$  moderate risk factor (age  $\geq 75$  years, hypertension, diabetes, and heart failure/LV systolic dysfunction)
6. Aspirin may be used for stroke prevention in patients without any risk factors.
7. Antithrombotic therapy (warfarin or aspirin) should be used on an individualized basis in patients with one moderate risk factor.
8. The international normalized ratio (INR) initially should be measured at least once per week and then once per month after a stable degree of anticoagulation when an INR of 2-3 is achieved.
9. When aspirin is used for stroke prevention, the daily dose should be 81-325 mg/day.
10. Patients with AFI should receive antithrombotic therapy in the same fashion as patients with AF.

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