



Clinical Guide - Stroke Prevention in Atrial Fibrillation

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Thrombosis in Atrial Fibrillation

Atrial Fibrillation (AF) creates hemodynamic disturbances which **lead to stasis** in the atria. This in turn may lead to **thrombus** formation.

Thromboembolism is a major complication of AF and may result in TIA, stroke or ischemia of an internal organ or an extremity.

Epidemiology of AF

AF is **frequent**⁽¹⁾. It is, in fact, the most common pathological tachycardia and is reaching epidemic proportions in the developed world. The prevalence increases with age: 0.2% below age 30 and over 12% at age 75 ⁽²⁾. The lifetime risk of developing AF is about 25%. Heart failure, hypertension and coronary artery disease are the predisposing factors most often associated with AF. Other strong associations are cardiomyopathies, mitral valve disease and hyperthyroidism.

The risk of stroke is approximately 4-5 % per year in non-rheumatic atrial fibrillation⁽³⁾ and is one of the most devastating consequences of AF.

What is Lone AF?

Lone atrial fibrillation is AF **without** structural disease, hypertension, diabetes or previous stroke. The risk of embolization is low in patients below 65 with lone AF.

Paroxysmal / Persistent AF

Intermittent or paroxysmal AF and persistent or permanent AF have the same risk for thromboembolic events and therefore **they should both be considered** for antithrombotic therapy.⁽⁴⁾

Risk stratification for embolization in AF. CHADS2 Score.

Congestive heart failure - 1 point

Hypertension - 1 point

Age > 75 years - 1 point

Diabetes mellitus - 1 point

Prior Stroke or TIA or embolism - 2 points

Estimating the risk of stroke at the bedside in non-valvular AF has been simplified by the use of the CHASDS2 score scheme. Patients are considered to be at low risk with a score of 0, at intermediate risk with a score of 1 or 2, and at high risk with a score of 3 or higher. Patients at low risk may be adequately treated with aspirin, 325 mg daily, those at intermediate risk with aspirin or warfarin, and those at high risk with warfarin (INR range 2-3).⁽³⁾

Atrial Fibrillation: Potential Candidates for Warfarin

- lone AF between age 65 and 74, and female gender and/or coronary disease.
- paroxysmal (intermittent) AF
- persistent or permanent AF
- thyrotoxicosis
- congenital heart disease
- valvular disease
- planned cardioversion

Age Alone Not Necessarily an Exclusion Criteria

The risk of stroke increases with age while the rate of bleeding of warfarin therapy is poorly correlated with age, below 80. In five trials, the overall bleeding complications with warfarin in older patients were similar to aspirin or placebo.^(3,4)

A patient should not be denied anticoagulation because of age alone. Because of the inconvenience of frequent INR monitoring, alternative antithrombotic therapy with low-dose warfarin plus aspirin, clopidogrel plus aspirin and ximelagratan have been tested. Warfarin has been superior to these alternative strategies in high risk patients, while aspirin is a reasonable option in low thromboembolic risk patients. Ongoing trials are evaluating the efficacy of other oral anticoagulants in AF, the direct thrombin inhibitors (DTI) and the direct Factor Xa (FXa) inhibitors that inhibit two important proteases in the coagulation cascade. These newer agents do not require laboratory monitoring. Dabigatran is the only oral DTI approved in Europe and Canada for primary prevention of venous thromboembolism, VTE. There are a number of FXa inhibitors undergoing clinical trials, and rivaroxaban and apixaban are in late stages of clinical development. Rivaroxaban is the first oral FXa inhibitor to be approved for clinical use in Europe for the primary prevention of VTE, and like dabigatran, could become the first agents in their respective classes of newer anticoagulants able to compete with and replace warfarin in AF patients, if ongoing studies nearing completion prove their benefits.

Poor Candidates for Warfarin

- contraindications to oral anticoagulation
- prone to fall
- unreliable/uncooperative

These patients should be considered for aspirin therapy although protection may be suboptimal

Major Bleeding is Rare

Major bleeding occurs in less than 2% of the anticoagulated AF patients per year, when target INR is monitored and maintained. The risk of bleeding is associated with the intensity of anticoagulation, concomitant use of aspirin and underlying disorders.

Prevention of stroke in AF

For every patient with AF, the treatment options include:

- electrical or pharmacologic conversion to sinus rhythm versus control of heart rate
- prevention of stroke using warfarin or aspirin.

Treatment must be individualized and based on estimates of patient benefit versus risk.

In an overview of the randomized trials, warfarin reduced the annual risk of stroke by 68% and aspirin reduced the risk by 36%⁽⁵⁾.

Initiation Made Easier...

- Initiate with maintenance dose of warfarin
- Maintain target INR 2.5 (range 2.0 to 3.0)
- If INR value outside therapeutic range and no signs or symptoms of thromboembolic complications or bleeding, have PT done again in 3 days. If necessary, then adjust the dosage +/- 1mg.
- Monitor regularly, about once every 4-6 weeks, when anticoagulation level is stable.

Safety of Warfarin Therapy⁽⁵⁾

Bleeding is the most important complication of anticoagulant therapy. The intensity of anticoagulation, the concomitant use of ASA, NSAIDs and the underlying clinical disorder, are major factors influencing the risk of bleeding.

Skin rash and **alopecia** are uncommon adverse effects and may be managed by changing oral anticoagulants.

Skin necrosis is a rare complication and usually appears within a few days of the start of oral anticoagulation therapy.

Drug interactions are the commonest cause of significant change in the INR value. Patients should be advised not to change any medication without a physician's or pharmacist's advice. Adequate monitoring is the key to a successful and safe warfarin therapy. Please refer to the T.I.G.C. brochure on warfarin therapy.

Emerging Therapy to prevent AF

Upstream therapy to prevent AF is an interesting and emerging area of research. Data to date suggest that ACE inhibitors and angiotensin-receptor blockers may be beneficial and the results of ongoing randomized trials are eagerly awaited. Other potentially useful therapies include the use of aldosterone antagonists, statins and fish oils. Non-pharmacologic approaches such as catheter ablation, surgery and pacing are also promising.

References:

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