

Battling Chronic Atrial Fibrillation in the Elderly

Despite being the most common sustained cardiac arrhythmia, affecting 5% to 9% of those over the age of 65, atrial fibrillation (AF) remains undertreated, leaving patients exposed to an unnecessarily high stroke risk. The authors discuss AF symptom control and stroke prevention.

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Janice's case

Janice, 78, has been controlling her lipids and blood pressure with medication over the past two years.

She presents with a four week history of fatigue, palpitations, and decreased appetite. She feels "over-medicated".



Her physical examination is unremarkable, except for a fast and irregular heart rate of 140 beats/minute. An electrocardiogram (ECG) shows rapid atrial fibrillation (AF).

For Janice's risk factors and lab results, go to page 32.

Atrial fibrillation (AF) is the most common, sustained cardiac arrhythmia. While < 1% of young adults are affected, the incidence increases to 5% to 9% in those over the age of 65.¹ Hypertension, mitral valve disease, and myocardial infarction resulting in left ventricular dysfunction are the most common causes of AF.

AF carries an increased risk of disabling strokes and a 50% to 90% increase in mortality, even after accounting for other cardiovascular risk factors.² Health care providers must attempt to control symptoms, minimize risk of stroke, and attempt to convert to sinus rhythm. Since the incidence of AF is expected to rise, given an aging population, proper management of this condition becomes crucial to prevent associated morbidity and mortality.

How can stroke be prevented?

Patients with AF experience a fivefold greater risk of stroke. A previous history of transient ischemic attack (TIA) or stroke, hypertension, diabetes, and female gender all increase risk of stroke in patients with concomitant AF. However, age remains the strongest risk factor, with Framingham data demonstrating the attributable risk of stroke from AF rising from 1.5% in 50- to 59-year-olds to 23.5% in 80- to 89-year-olds.³ Table 1 outlines the annual rate of stroke in patients with AF.

A meta-analysis investigating stroke prevention in AF demonstrated that warfarin decreas-

Table 1

Annual rate of stroke in patients with AF

Age	Risk category*	Annual stroke rate
< 65 years	No risk factors	1.0
	One or more risk factors	4.9
65-75 years	No risk factors	4.3
	One or more risk factors	5.7
> 75 years	No risk factors	3.5
	One or more risk factors	8.1

* Risk factors: history of hypertension, diabetes mellitus, or prior stroke/transient ischemic attack.

es the risk of stroke by 62% and 36% compared to placebo and acetylsalicylic acid, respectively.⁴ The protective effects of warfarin are even more pronounced in elderly patients, especially those with additional risk factors for stroke. Pooled data from five randomized, controlled trials indicate that, for patients over 75, warfarin decreases the annual rate of stroke from 3.5% to

One study showed only 20% of patients over 75 were being adequately treated.

1.7% for those without added risk factors. In those with a minimum of one added risk factor, the rate of stroke decreases from 8.1% to 1.2%, a staggering 85% reduction in stroke annually.⁵

What are the risks of anticoagulation?

Despite the known benefits of anticoagulation in the elderly, studies continue to demonstrate that warfarin is underused in high-risk patients.

Table 2A

Outpatient bleeding risk index

1. Add risk factors for major bleed on warfarin
 - Age > 65
 - History of stroke
 - History of gastrointestinal bleed
 - The presence of one or more of:
 - Recent myocardial infarction
 - Renal insufficiency (serum creatinine > 1.5 mg/dL)
 - Diabetes mellitus
2. Sum risk factors
3. Classify patient (Table 2B)

One European study showed only 20% of patients over 75, with no contraindications to anticoagulation, were being adequately treated.⁶ The cost, inconvenience, and fear of major bleeds prevent patients and health care providers from initiating anticoagulation.

A large prospective trial of 1,100 patients with AF examined the risk of major bleeding in patients on warfarin. The annual risk of major bleeding, found to increase significantly with higher international normalized ratios (INR), increased from 1.7% in patients 75 years and younger to 4.2% in those older than 75.⁵

Besides age and the intensity of anticoagulation, other risk factors for anticoagulation-associated bleeding have been described.

A meta-analysis of elderly patients concluded the only absolute contraindications to anticoagulation include bleeding diathesis and thrombocytopenia of platelets < 50 x 10³/μL.⁷ Sustained hypertension (> 160/90 mmHg) contraindicates the use of anticoagulation due to the increased risk of intracerebral hemorrhage; however, appropriate blood pressure control eliminates this risk factor.

Non-compliance with medication and INR monitoring are other absolute contraindications.

Table 2B

Outpatient risk classification

	0 risk factors	1-2 risk factors	3-4 risk factors
Risk	Low	Intermediate	High
Estimated risk major bleed 12 months	3%	8%	30%
Estimated risk major bleed 48 months	3%	12%	53%

While this can be of particular concern for patients with dementia, moving to a supervised environment or enlisting family and community services for supervision mitigates the risk.

Exciting new oral anticoagulants, such as the direct thrombin inhibitor, ximelagatran, exhibit a more predictable magnitude of action than warfarin and do not require INR checks. This medication is currently undergoing testing.

Pooled data from the two trials investigating ximelagatran versus warfarin in AF patients demonstrate an equal reduction in stroke, equal risk of bleeding, but increased incidence of transient increase in liver enzymes with ximelagatran.⁸

Alcohol abuse predisposes patients to a 2.6 times increased risk of anticoagulation-related bleeding; therefore, alcohol intake should be reduced to two drinks/day before initiating therapy. Non-steroidal anti-inflammatory drugs

(NSAIDs) increase the risk of gastrointestinal bleeding with warfarin, but using a cyclooxygenase-2 inhibitor-specific NSAID, or adding a proton pump inhibitor, reduces the risk.

Propensity to falling does not increase the

risk of anticoagulation-related bleeds. In such patients, an analytic decision model demonstrated that a patient's propensity to fall does not eliminate the benefit of anticoagulation since the risk of stroke was far greater than the rate of subdural hematomas (SDH) caused by falls; in fact, the model concludes an individual must fall 295 times/year for the risk of a SDH to outweigh the benefit of stroke reduction with warfarin.

Beyth, *et al.* developed a scoring system to assess the patient's risk of bleeding before starting warfarin treatment (Tables 2A & B).⁹ Interestingly, the system predicted a patient's risk significantly better than physicians' estimates. Several bleeds occurring in high-risk patients were possibly preventable by avoiding antiplatelet medications, supratherapeutic INRs, and holding warfarin for invasive procedures.

Unfortunately, some factors that increase the risk of stroke, such as advanced age and history of stroke, also increase the risk of major bleeding.

About the author...

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How are symptoms controlled?

In a study of 756 patients with AF, 16.2% of patients complained of symptoms, the most common being dyspnea (46.8%) and palpitations (44.7%).¹ Cardiac output in patients with

Janice's risk factors and lab results

Risk factors

- Cardiovascular disease and diabetes are absent
- Hyperlipidemia is controlled
- Hypertension is controlled (135/70 mmHg)
- Family history is negative (brother had a stroke late in life [in his 70s])
- Non-smoker
- Consumes 3 to 4 alcoholic drinks/week
- Exercise is limited because of arthritis

Lab investigations

- Normal thyroid-stimulating hormone levels
- Echocardiogram: AF heart rate between 100-160 beats/minute over 24 hours
- Normal Holter
- Electrolytes, blood urea nitrogen, creatine, liver function tests, and magnesium are normal
- Normal chest X-ray

For more on Janice, go to page 33.

AF is compromised at ventricular rates > 90 beats/minute, with studies demonstrating increased symptoms at faster heart rates.

Several therapeutic options exist to decrease ventricular rate:

- While digoxin decreases heart rate by increasing vagal tone, it is often ineffective, especially during exercise.
- Atrioventricular (AV) node-blocking agents, including beta-blockers and calcium channel blockers (*i.e.*, diltiazem and verapamil), are other options.
- A systematic comparison crossover trial of five common pharmacologic regimens for rate control in 12 patients (mean age of 69)

with AF concluded that the most effective rate control at rest and exercise was achieved with a combination of atenolol and digoxin.

- Single-agent treatments with digoxin or diltiazem alone were found to be the least effective.

What about sinus rhythm?

Conversion to sinus rhythm is another option for symptom control. Electrical cardioversion can restore sinus rhythm at least temporarily, in 80% to 90% of patients with AF.¹⁰ Ideally, patients receive warfarin therapy for three to four weeks prior to cardioversion. Recurrent AF often requires suppression with antiarrhythmic medication.

Although several antiarrhythmic medications are effective, not all are recommended. A meta-analysis of quinidine demonstrated a threefold increase in mortality. Currently, amiodarone has been demonstrated to be the most beneficial medication for maintaining sinus rhythm.

In a large, randomized trial of 403 patients, amiodarone was associated with a 57% reduction in the risk of AF recurrence, compared to treatment with either sotalol or propafenone after a 16-month followup. This benefit persisted in those over 65 years of age.

If amiodarone therapy is decided upon, patients must be monitored for side-effects, including:

- hepatotoxicity,
- pulmonary fibrosis,
- hypothyroidism or hyperthyroidism,
- photosensitivity, and
- arrhythmias.

Followup on Janice

Janice's risk of cardiovascular accident is high. Heart rate control and anticoagulation are key to her management. Antiarrhythmics should be reserved for uncontrolled symptoms only.

While she feels over-medicated, digoxin and beta blocker therapy are required to control her rapid AF. Warfarin therapy is also initiated, aiming for an INR of 2.5.

Janice is doing well and is protected against future stroke.

Rate versus rhythm control

The debate over whether to attempt rhythm conversion or merely control ventricular rate has been a heated topic, with little evidence backing either argument. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial shed new light on the debate.

The trial, which randomized elderly chronic AF patients to attempted maintenance of sinus rhythm or to treatment with rate-controlling drugs, clearly demonstrated that rhythm control offers no survival advantage over rate control after a mean followup of 3.5 years. Moreover, patients in the rhythm-control group required more hospitalizations and suffered more adverse drug reactions. There was no difference in the number of ischemic strokes between the two groups; 70% of patients in the rhythm-control group continued on warfarin. The majority of strokes occurring during the trial were due to discontinuing warfarin or a subtherapeutic INR.


In general, attempting rhythm control offers no benefit to rate control in chronic AF with respect to mortality, morbidity, incidence of strokes, and quality of life.

What does it all mean?

AF is a chronic, recurrent problem undertreated by physicians, particularly in elderly people who are subsequently being exposed to an unnecessarily high stroke risk. Chronic heart failure can result without adequate ventricular rate control, and if AV blocking and vagolytic agents are not effective, AV nodal ablation with pacemaker should be considered.

Until recently, there was little evidence to guide physicians on the benefits of ventricular rate versus rhythm control. The AFFIRM trial concluded that rate control confers similar mortality and improved morbidity compared to rhythm control.

In patients who cannot tolerate AF, rhythm control may be required; amiodarone has been demonstrated to be the best medication to maintain sinus rhythm. Patients on amiodarone should be on a low dose, 200 mg/day, and should be instructed to protect themselves from sun exposure and have thyroid-stimulating hormone and liver function tests two to four times/year.

The majority of patients with AF are elderly and either asymptomatic or mildly symptomatic. These patients should receive adequate rate control and should be anticoagulated unless contraindications to oral anticoagulant therapy are present. Anticoagulation has been shown to decrease risk of stroke and prevent the associated morbidity. 

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Take-home message

- A previous history of transient ischemic attack (TIA) or stroke, hypertension, diabetes, and female gender all increase risk of stroke in patients with concomitant AF.
- Despite the known benefits of anticoagulation in the elderly, studies continue to demonstrate that warfarin is underused in high-risk patients.
- Attempting rhythm control offers no benefit to rate control in chronic AF with respect to mortality, morbidity, incidence of stroke, and quality of life.

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