Update on the Management of Atrial Fibrillation in Older Adults

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Atrial fibrillation (AF) is by the far the most common cardiac rhythm disturbance encountered in clinical practice. It is associated with significant morbidity and mortality and has potentially lifelong implications in terms of therapy and complications. This disease is more commonly seen now given the increased life expectancy and the remarkable advances made in health care. The already at-risk older adult population is particularly vulnerable to complications from AF, especially embolic cerebrovascular events. This article reviews the evidence-based management of AF with a particular focus on the older adult population.

Key words: *atrial fibrillation, older adults, stroke, rate control, rhythm control, stroke prophylaxis, anticoagulation*

Case

A 77-year-old man presented with hypertension and a previous right-middle cerebral artery ischemic stroke with mild residual left-sided motor weakness. He was found to have an irregular heartbeat, with a radial rate ranging between 90 and 110 beats per minute. His examination was remarkable for an irregularly irregular pulse with a blood pressure of 150/90 mm Hg. His transthoracic echocardiogram showed normal left ventricular systolic function with impaired relaxation consistent with diastolic dysfunction. His initial laboratory investigations including a thyroid profile were unremarkable. What is your approach to the management of this patient?

Background

Atrial fibrillation (AF) is commonly encountered in clinical practice, be it in an outpatient office setting or in the context of a busy inpatient service.[1] It is also the commonest arrhythmia encountered in a critical care unit and in the postoperative setting following cardiac and noncardiac surgeries. The incidence of AF in the community increases with age, approaching 8% in the population over 80 years of age.[1] Of note, the incidence has been on the rise, even after adjusting for age. This likely reflects a rising trend in the disease conditions associated with AF such as hypertensive heart disease. The condition is 1.5 times more commonly seen in males than in an age-matched female population.[2]

Advancing age is a well-recognized risk factor for stroke. About 75% of all strokes occur in individuals over 65 years of age. According to U.S. stroke data, the risk of having a stroke more than doubles for each decade over 55 years of age.[3] Combining this with the increased risk of AF among older adults places this vulnerable segment of the population at a significantly increased risk of stroke, adding a growing burden to our health care system. In addition, the Framingham Heart Study showed that AF is an independent risk factor for death resulting in a 1.5- to 1.9-fold increase in mortality associated with systemic embolic events, cerebral embolic events, and heart failure.[4]

Due to the devastating implications of AF in the general population and the older adult population, in particular, a sound understanding of the management of AF and the evidence supporting it is of paramount importance to contemporary practitioners.

Classification and Etiology

The classification of AF follows the temporal pattern within which it is identified. It can be a single isolated or recurrent event. This is further classified into paroxysmal, with episodes that revert back to sinus rhythm within 7 days, typically in the first 48 hours in 60% of the cases; persistent, with episodes lasting longer than 7 days; and permanent, referring to episodes that last for more than a year, regardless of whether cardioversion was attempted or not.

A comprehensive evaluation for an underlying etiology associated with AF should take into consideration the various cardiac and noncardiac conditions with which AF may be linked. Table 1 outlines such disease states.

Hemodynamic Consequences

In AF, disorganized atrial activity leads to the loss of atrial contribution to the left ventricular stroke volume, which may lead to a significant drop in left ventricular output in certain disease states. In addition, the rapid ventricular rates interfere with the diastolic filling of the left ventricle, further reducing cardiac output. The results of these hemodynamic changes are more marked in conditions associated with impaired diastolic ven-

Table 1: Causes of Atrial Fibrillation

Cardiac	Noncardiac
Hypertensive heart disease	Endocrine pathology—hyperthyroidism, pheochromocytoma, obesity
Ischemic heart disease	Neurological pathology—ischemic infarcts, subarachnoid hemorrhage
Valvular heart disease—MS, MR, MVP, AS	Pulmonary pathology—pneumonia, ARDS, pulmonary embolism, ILD
Cardiomyopathy—dilated, infiltrative, e.g., amyloidosis, hemochromatosis, hypertrophic, myocarditis	Post–noncardiac surgery
Pericardial pathology—pericarditis, myopericarditis, tumours with pericardial involvement	Toxins—alcohol, caffeine, stimulants
Postcardiac surgery	Obstructive sleep apnea
Electrophysiological abnormalities—enhanced automaticity, conduction abnormality (re-entry), sick sinus syndrome	"Lone" atrial fibrillation
Congenital heart disease—ASD, VSD	

ARDS = acute respiratory distress syndrome; AS = aortic stenosis; ASD = atrial septal defect; ILD = interstitial lung disease; MR = mitral regurgitation; MS = mitral stenosis; MVP = mitral valve prolapse; VSD = ventricular septal defect.

tricular relaxation, as seen with advancing age, hypertensive heart disease, and hypertrophic cardiomyopathy.

The increase in the risk of stroke is related to the formation of intracardiac thrombi, typically in the left atrial appendage. These can be identified as early as 24–48 hours after the onset of AF. Interestingly, in about 25% of cases, the source of an embolism may be the left ventricle, the valves, or the major arteries.[5]

Rhythm Control versus Rate Control

Rate control targets the slowing of rapid ventricular rates and the alleviating of the discomfort associated with symptomatic palpitations. In doing so, it also prevents tachycardia-induced cardiomyopathy. Rate control can be effectively achieved using atrioventricular nodal blockers such as beta-blockers and nondihydropyridine calcium channel blockers such as diltiazem. These agents are effective in controlling heart rate both during exertion and at rest. Digoxin has fallen out of favour due to its limited efficacy in controlling a sympathetically driven increase in heart rate, for example, during exercise. Its use now is limited to controlling the ventricular rate in AF associated with symptomatic left ventricular systolic dysfunction, usually as an adjunct.

On the other hand, rhythm control can be achieved chemically or electrically. The most effective pharmacological agents in restoring sinus rhythm are amiodarone, dofetilide, ibutilide, dronaderone[6] (Vaughan Williams class III), flecainide (Vaughan Williams class IC), and propafenone (Vaughan Williams class IA).[7] With the advent and evolution of interventional cardiac electrophysiology, pulmonary vein isolation is now associated with a 70–75% success rate in restoring sinus rhythm. The procedure carries a 3–6% risk of a substantial complication such as pulmonary vein stenosis or atrioesophageal fistula. The risk is considerable knowing that more than one attempt may be required to achieve sinus rhythm.[5]

There is abundant literature from a multitude of trials that have examined the efficacy and long-term outcomes associated with either approach. Table 2 summarizes the characteristics of landmark trials of rhythm versus rate control in AF.

When comparing the two approaches, there was no statistically significant difference in morbidity and mortality between rhythm and rate control in AF.[8–12] In fact, the largest of the studies suggested a trend toward an increase in mortality in the rhythm control arm, partly related to toxicity from antiarrhythmic medications.[8] Therefore, patients should be carefully evaluated to determine suitability for either approach. Generally, a rate control strategy is the mainstay of treatment in older adults. This minimizes the risk of adverse drug interaction that is coupled with polypharmacy, a major geriatric giant, and also reduces the risk of exposure to the toxic side effects of antiarrhythmic medications. Table 3 outlines the patient characteristics that may aid in deciding the most appropriate treatment strategy, and Table 4 summarizes the advantages and disadvantages of each approach.

Risk of Stroke and Thromboprophylaxis

The risk of an embolic stroke in individuals with nonvalvular AF is three- to fivefold the risk in an age-matched population in sinus rhythm. This risk grows exponentially in association with valvular pathology, for example, mitral

stenosis, up to 15- to 17-fold. All types of AF are uniformly linked to this complication.[13,14] A number of scoring systems have been devised to risk stratify patients and determine the optimum antithrombotic therapy. The most popular and well-validated scoring system is the CHADS2 score[15] (Congestive heart failure, Hypertension, Age ≥75 years, Diabetes, prior Stroke/transient ischemic attack/systemic embolism; Figures 1 and 2). Females are at greater risk of stroke compared with an age-matched population of males, even after adjusting for other risk factors.[16,17] The most potent predictor of risk for embolization in nonvalvular AF is a history of previous embolic events. Accordingly, the annual risk of stroke without antithrombotic treatment approaches 12%.[18]

Age has a substantial impact in determining the risk of future embolic events. The annual risk approaches an alarming 25% in patients with AF who are past the eighth decade.[4] Embolic strokes in AF carry a poor prognosis as the infarcts tend to be larger and associated with more severe neurological deficits and a greater tendency for a hemorrhagic transformation.[17]

There is strong evidence from all the major trials addressing stroke prevention in AF supporting the use of antithrombotic agents for primary and secondary prophylaxis.[18–24] The relative risk is reduced by 64% with international normalized ratio (INR)-dose adjusted warfarin therapy and by 22% with acetylsalicylic acid (ASA) therapy alone.

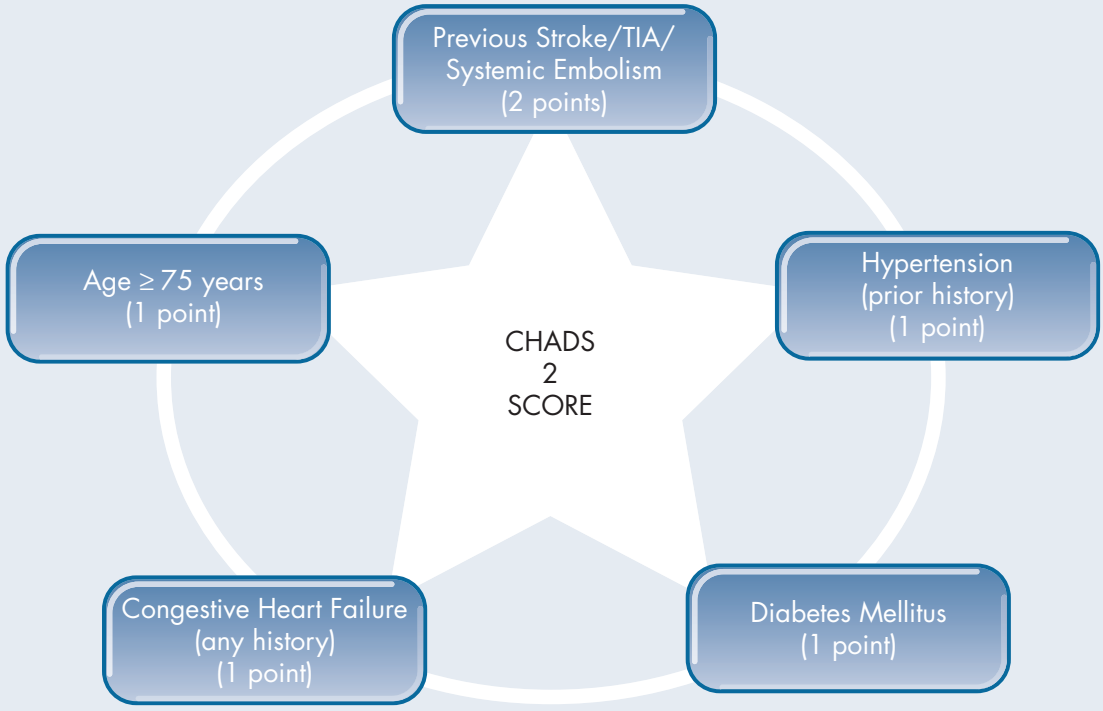
Table 2: Summary of Major Trials Comparing Rhythm Control versus Rate Control in Atrial Fibrillation

						Patients Reaching Primary End Point (n)		
Trial	**Patients (n)**	**Mean Age (y)**	**Mean Length of Follow-Up (y)**	**Inclusion Criteria**	**Primary End Point**	**Rate Control**	**Rhythm Control**	**p**
PIAF (2000)	252	61.0	1.0	Persistent AF (7–360 d)	Symptomatic improvement	76/125 (60.8%)	70/127 (55.1%)	.317
RACE (2002)	522	68.0	2.3	Persistent AF or flutter for <1 y and 1–2 cardioversions over 2 y and oral anticoagulation	Composite: cardiovascular death, CHF, severe bleeding, PM implantation, thromboembolic events, severe adverse effects of antiarrhythmic drugs	44/256 (17.2%)	60/266 (22.6%)	.11
STAF (2002)	200	66.0	1.6	Persistent AF (> 4 wk and <2 y), left atrial size >45 mm, CHF NYHA II–IV, LVEF <45%	Composite: overall mortality, cerebrovascular complications, CPR, embolic events	10/100 (10.0%)	9/100 (9.0%)	.99
AFFIRM (2002)	4,060	69.7	3.5	Paroxysmal AF or persistent AF, age 65 y or older, or risk of stroke or death	All-cause mortality	310/2,027 (25.9%)	356/2,033 (26.7%)	.08
HOT CAFÉ (2004)	205	60.8	1.7	First clinically overt episode of persistent AF (7 d or more and <2 y), 50–75 y old	Composite: death, thromboembolic complications, intracranial or other major hemorrhage	1/101 (1.0%)	4/104 (3.9%)	>.71

AF = atrial fibrillation; AFFRIM = Atrial Fibrillation Follow-up Investigation of Rhythm Management; CHF = congestive heart failure; CPR = cardiopulmonary resuscitation; HOT CAFÉ = How to Treat Chronic Atrial Fibrillation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PIAF = Pharmacological Intervention in Atrial Fibrillation; PM = pacemaker; RACE = Rate Control Versus Electrical Cardioversion for Persistent Atrial Fibrillation; STAF = Strategies for Treatment of Atrial Fibrillation.

Source: Reproduced with permission from Fuster V et al., 2006.[7]

Figure 1:
CHADS2 Score for Assessing Stroke Risk in Patients with Atrial Fibrillation and Suggested Thromboembolic Prophylaxis



0	• Adjusted stroke rate 1.9% per year • ASA 81-325 mg daily for prophylaxis
1	• Adjusted stroke rate 2.8% per year • ASA 81-325 mg daily or warfarin with target INR 2.5 (2-3)
2	• Adjusted stroke rate > 4% per year • Warfarin with target INR 2.5 (2-3)
3	• Adjusted stroke rate 5.9% per year • Warfarin with target INR 2.5 (2-3)
4	• Adjusted stroke rate 8.5% per year • Warfarin with target INR 2.5 (2-3)
5-6	• Adjusted stroke rate 12.5-18.2% per year and increases with more points • Warfarin with target INR 2.5 (2-3)

ASA = acetylsalicylic acid; INR = international normalized ratio; TIA = transient ischemic attack.

Table 3: Clinical Characteristics Favouring Rhythm Control versus Rate Control in Individuals with Atrial Fibrillation

Factors Favouring Rate Control	Factors Favouring Rhythm Control
Persistent AF	Paroxysmal AF
Recurrent AF	First episode
Rhythm well tolerated (asymptomatic)	Rhythm not well tolerated (symptomatic)
Age ≥65 yr	Age <65 yr
Hypertension	No hypertension
No history of CHF	History of CHF (to restore atrial kick)
Previous antiarrhythmic drug failure	No previous exposure to antiarrhythmic therapy
Patient preference	Patient preference

AF = atrial fibrillation; CHF = congestive heart failure.

Most of the current guidelines caution against combining the two agents for this indication due to a higher risk of major hemorrhage without an added protective effect. For individuals with contraindications to oral anticoagulants, there is now evidence that dual antiplatelet therapy with ASA and clopidogrel provides a greater protection from embolic stroke when compared with ASA therapy alone.[25,26]

The older adult population perhaps benefits the most from anticoagulation and, yet, is at most risk for bleeding complications. The overall risk of a major bleed is estimated to be 3–4% per year with warfarin compared to 0.5–1% per year with ASA.[27] This risk is largely offset by the devastating impact of an embolic stroke. As a result, oral anticoagulation with warfarin remains the standard recommendation in preventing thromboembolic events even in the very old.[28,29] Despite this, warfarin is seriously underused in this age group, with prescription rates approaching only 40%.[30,31] This reluctance stems from concerns about precipitating a major bleed in a frail older adult. Moreover, the inconvenience of frequent blood tests, access to laboratories, potential for drug interactions are all confounding factors. The risk of falls is probably a major determinant of withholding anticoagulants in older patients with AF, mainly due to increased concomitant risk of developing subdural or intracranial hemorrhage. Several studies have addressed the authenticity of this concern. They uniformly concluded that a risk of falls should not preclude an older patient with AF from being anticoagulated with warfarin.[31,32] This was based on the observation that the risk of developing a subdural, while on anticoagulants was small compared with the

Table 4: Advantages and Disadvantages of Rate Control versus Rhythm Control in Patients with Atrial Fibrillation

Rhythm Control		Rate Control	
Pros	**Cons**	**Pros**	**Cons**
Improves symptoms by restoring sinus rhythm	Increased risk of adverse drugs reactions secondary to the use of antiarrhythmic agents	Effective agents for rate control and less toxic compared with antiarrhythmic agents	Need for therapeutic anticoagulation
Improves exercise tolerance	Modest efficacy in maintaining sinus rhythm[8]	Rapid relief of symptoms	No difference in mortality/ morbidity, especially risk of stroke, compare with rhythm control
Less need for anticoagulation	Increased risk of hospitalization for recurrent AF and cardioversion	More cost effective	
Improved hemodynamics by restoring atrial kick	No difference in future risk of stroke compared with rate control		

Key Points

Atrial fibrillation (AF) is a common clinical problem among older adults. The disease, its complications, and its therapy have serious implications for the well-being of the patient.

Atrial fibrillation can be seen in association with cardiac and noncardiac conditions. It may be the presenting feature in certain diseases such as hyperthyroidism and hemochromatosis.

Rate control is the preferred and likely the least toxic management strategy in older adults.

All forms of AF are associated with an increased risk of stroke.

Barring major deterrents, oral anticoagulation should always be recommended to older adults with AF for primary and secondary prophylaxis against embolic events.

risk of an embolic stroke. It was estimated that an older person with atrial fibrillation with an average risk for stroke (4% per year) must sustain 300 falls per year before the risk of a major subdural bleed counterbalances the protective effect.[32] Every effort should be made to identify and rectify any possible predisposition to bleeding while on anticoagulant therapy. Psychomotor impairment and declining cognitive function, postural instability and risk of falls, access to INR monitoring, and drug interactions with oral anticoagulants all factor into the decision to assign anticoagulation therapy to an older adult with AF. While advancing age is a major predictor of such complications, the combination with antiplatelet agents, previous stroke, and uncontrolled hypertension are also important.[28,7]

Summary

Atrial fibrillation is a major health care issue among older adults. Both the disease and its treatment are accompanied by major implications to the well-being of the older person. Hence, a careful evaluation of the clinical situation is desired to contrast the risks and benefits of therapy in this frail population.

Case Resolution

Our patient is found to be in asymptomatic AF. He will benefit from rate control with beta-blockers. His CHADS2 score of 4 places him at high risk for future embolic events. After careful assessment of his risk for bleeding, lifelong anticoagulation should be recommended to reduce this risk.

When evaluating an older patient for anticoagulation, the standard risk scoring systems apply. In addition, a comprehensive overview of the factors increasing the risk of major bleeding with anticoagulant therapy should also be undertaken given the susceptibility to this complication. This includes a screening cognitive assessment, an assessment of gait and risk of fall, an evaluation of the need for concomitant therapy with antiplatelet agents for other indications, adequate blood pressure control, and a careful evaluation for a possible interaction between oral anticoagulants and other medications that the patient might be taking.

Clinical Pearl

A reasonable and safe strategy in the management of AF in older adults should focus on rate control and anticoagulation. This recommendation stems from the consistent absence of a demonstrable advantage of rhythm control and also the increase in trend toward adverse events and mortality related to the toxicities associated with antiarrhythmic therapy. This has special relevance in a population with an increased incidence of underlying structural heart disease.

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