

CLINICAL REVIEW

Atrial Fibrillation: A Review of Management and Stroke Prevention

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ABSTRACT

Atrial fibrillation (AF) is the most common cardiac arrhythmia in adults. Common etiologies of AF include cardiac causes (hypertension, ischemia/infarction, valvular heart disease) and non-cardiac causes (hyperthyroidism, excess alcohol consumption and pulmonary embolism). The American Heart Association estimates that a quarter of all strokes each year are related to AF. The purpose of this review is to evaluate current guidelines relating to risk stratification and treatment options for anticoagulation therapy for stroke prevention in the setting of AF. In the acute management of AF, there is ongoing debate as to whether rate control or rhythm control should be the primary therapeutic goal. For chronic AF, however, the main therapeutic goal is to achieve optimal anticoagulation in order to reduce the risk of thromboembolic stroke.

INTRODUCTION

Atrial fibrillation (AF), a type of supraventricular tachycardia, results from the uncoordinated firing of electrical impulses from multiple sites in the atria, which can lead to ineffective pumping of the heart and an irregularly irregular pulse.¹ The consequences of atrial fibrillation depend on the underlying condition of the heart and is an independent risk factor for death.¹ Most episodes of AF are asymptomatic, being solely detected via ambulatory (“Holter”) ECG monitoring.¹

The irregular, rapid heart rate in AF has been shown to induce left and right atrial dilatation, which may lead to functional tricuspid and mitral regurgitation as well as left ventricular dysfunction.² In a healthy heart, stroke volume is dependent on preload, afterload, and the contractility of the heart. Preload varies with the venous return to the right atrium, while afterload depends on the resistance against which the left ventricle pumps.³ The stroke volume can be compromised in AF by up to 20% due to ineffective filling from the atrial.^{1,4} Decreased stroke volume ultimately results in structural changes that can cause ventricular dysfunction.^{1,4} Since both heart rate and stroke volume are affected in AF, the cardiac output is often compromised.

Although management of AF has been shown to prevent contractile dysfunction that leads to decreased cardiac out-

put, the main impetus driving management is a desire to prevent thromboembolic events.¹ Over time, uncoordinated contractions that occur during episodes of AF allow for blood stasis, thrombus formation in the left atrial appendage, and ultimately embolization, especially upon reversion to normal sinus rhythm.¹ Cardiogenic emboli that result in stroke most often lodge in the medial cerebral artery (MCA), the posterior cerebral artery (PCA), or one of their branches, depending on their size.³ An embolus measuring 3-4 mm can occlude the stem of the MCA, resulting in a large infarct involving both gray and white matter.³ Smaller emboli may occlude small cortical or penetrating arterial branches.³ The extent of the collateral circulation determines the location and size of the infarct within a vascular territory.³

This paper will focus on guidelines for the treatment and management of AF. We will review the AFFIRM study that deals with the debate between rate-control versus rhythm-control for treatment.⁵ We will also discuss the use of anticoagulation therapy in preventing strokes.

ETIOLOGY

The prevalence and incidence of AF increase with age, as demonstrated in the ATRIA study, which showed that 70% of AF patients were at least 65 years old.⁶ Aging leads to an increase of fibrous and adipose tissue deposition in the SA

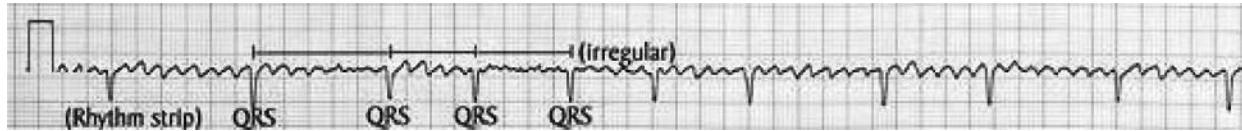


Figure 1. An ECG strip demonstrating the typical pattern seen in AF.¹

node and ventricles. The incidence of AF also increases with the presence of coronary artery disease and hypertension.⁷

AF is associated with atrial pathologies such as atrial enlargement, elevated atrial pressure and atrial inflammation, as well as heart failure, according to the Framingham Heart Study.⁷ The cardiovascular conditions associated with AF include acute myocardial infarction (MI) (6-10%), heart failure (10-30%), and hypertrophic cardiomyopathy (10-30%).⁸ Surgical procedures, especially coronary artery bypass grafting (30-40%) and cardiac valve procedures (37-50%), are also associated with AF.⁸ Non-cardiac conditions associated with AF include pulmonary embolism (10-14%), hyperthyroidism (8.3%), and AF triggered by heavy alcohol consumption, which often occurs after a weekend or holiday and is thus termed “holiday heart syndrome” (60%).⁸

Two mechanisms have been postulated for AF. The first and most common mechanism implicates multiple small reentrant circuits in the atria that enter a cycle of generating, terminating, and then reemerging electrical activity. The second mechanism involves a rapidly-firing ectopic focus or foci, usually located near the pulmonary veins, that may degenerate into AF after brief bursts of aberrant activity.¹

CLINICAL PRESENTATION AND DIAGNOSIS

Patients with AF may present at any point along a spectrum of symptoms, from completely asymptomatic to experiencing chest pain, dyspnea, dizziness and fatigue.^{1,4} Patients may perceive any irregular rhythm, whether fast or slow, as “palpitations,” but these sensations are not necessarily pathognomonic for AF.^{1,4} AF is classified as acute if its symptoms have been present for less than 48 hours, chronic otherwise.⁹

Several physical examination findings raise one’s suspicion of AF: the cardiac rhythm is rapid and irregularly irregular, and the first heart sound usually varies in intensity.³ On the jugular venous pulse, there is loss of a waves (atrial contraction waves).³ The carotid artery exhibits variability in pulse pressures.³ Depending on associated heart conditions, the patient may also exhibit signs such as dependent pitting edema, coarse crackles at the bases of both lung fields and a raised jugular venous pressure (more than 4 cm above the sternal angle).¹⁰

ECG Findings

AF is usually diagnosed by its characteristic ECG pattern, as shown in Figure 1, demonstrating a rapid irregular tachycardia with absent P waves.¹ The QRS complexes are narrow (shorter than 0.12 s in duration). The atrial frequency ranges from 350 to 600 beats per minute, and the ventricular response is irregular.³

TREATMENT

Treatment of AF is important because of the potentially serious complication of embolic cerebrovascular accident (CVA). In patients without anticoagulation, the incidence of CVA averages 5% per year.^{11,12} The identified risk factors for CVA, found through multivariate analysis of pooled data, can be found in Table 1.

Table 1. Risk Stratification and anticoagulation in non-valvular AF¹³

1. High risk (annual risk of CVA without anticoagulation = 8-12%)

- All patients with previous transient ischemic attack or CVA
- All patients aged 75 years and over with diabetes and/or hypertension
- All patients with clinical evidence of valve disease, heart failure, thyroid disease, and/or impaired left ventricular function on echocardiography

2. Moderate risk (annual risk of CVA without anticoagulation = 4%)

- All patients aged under 65 years with clinical risk factors: diabetes, hypertension, peripheral arterial disease, ischemic heart disease
- All patients aged over 65 years who are not in high-risk group

3. Low risk (annual risk of CVA without anticoagulation = 1%)

- All other patients under 65 years with no history of embolism, hypertension, diabetes, or other clinical risk factors.

In the acute setting, AF can be treated by imposing rate control or rhythm control. Although the decision between rate control with drugs or rhythm control with either drugs or cardioversion has been debated, the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) and Rate Control versus Electrical Cardioversion (RACE) studies showed no difference in benefit with respect to rates of death or embolic stroke.¹³ In both groups, the annual incidence of strokes was about 1%, and strokes occurred mostly in patients who had stopped their warfarin or when the INR level was sub-therapeutic.¹⁴ Treatment of AF is summarized in Table 2.

Rate Control

In patients with AF, heart rate control through pharmacological methods prevents the onset of tachycardia during daily activities.¹ Rate-controlling agents include cardiac glycosides such as digoxin, beta-blockers, and calcium channel blockers (CCBs). One main difference between these agents is that the maximum effect of digoxin may not occur for several hours, whereas beta-blockers and CCBs produce more rapid rate control.¹

Rhythm Control

Rhythm control can be achieved by either pharmacological methods or by electrocardioversion.^{4,15} No studies to date have compared the two methods of rhythm control. However, in patients with AF that has lasted less than 48 hours, early drug therapy to restore sinus rhythm has shown to be beneficial, and increases the likelihood of conversion to as much as 90%.¹

Direct-current cardioversion, on the other hand, is indicated in two groups of patients. The first group is stable patients experiencing persistent AF (>7 days) who may undergo elective cardioversion after adequate anticoagulation has been established.¹ The second group is unstable patients with AF of recent onset experiencing unstable angina, acute pulmonary edema, and/or acute MI, who should undergo urgent cardioversion in order to prevent the devastating consequences of systemic hypoperfusion.¹

In patients with AF of greater than 48 hours' duration, it is imperative to administer anticoagulation before attempting cardioversion to reduce the risk of causing a thromboembolic complication.¹ By contrast, there is no evidence to support a need to anticoagulate prior to electrical cardioversion in new-onset AF (less than 48h).¹⁶ Two approaches may be taken. The first is to anti-coagulate as an outpatient with warfarin until an INR of 2-3 has been reached for a minimum of 3 weeks, then cardiovert. The second is to perform early cardioversion provided that a transesophageal echocardiogram (TEE) shows no intracardiac thrombi. Studies have shown an extremely low rate of thromboembolism after cardioversion when a TEE had indicated an absence of thrombus.⁴

The main disadvantage of the rhythm control strategy is that it is only temporarily effective: many patients spontaneously revert to AF.¹⁷ After direct current cardioversion, only 25% of patients remain in sinus rhythm after one year, compared to 50-75% who received pharmacologic cardioversion.⁴ At the time when patients spontaneously revert to AF, they are at increased risk of embolic events.^{3,17,18,19}

A recent report from Ottawa suggests that an aggressive protocol of IV procainamide followed by electrical cardioversion (as needed) was over 90% successful in restoring normal sinus rhythm and facilitating ED discharge with cardiology follow-up (n=660, mean duration of AF = 8.9hrs). Although 8.7% of patients reverted to AF within 7 days, there were no reports of stroke or death during the five-year study period.²⁸

A recent Cochrane review studied the role of anti-arrhythmics for maintaining sinus rhythm after cardioversion of AF and evaluated the risks (including mortality) and benefits. They concluded that there were no clear long-term benefits with the use of anti-arrhythmic drugs.²⁰

Surgical Options

Due to their negative inotropic effects, rate-control drugs are not the best option in patients who have systolic dysfunction in addition to atrial fibrillation. In such cases, surgical intervention is indicated. Surgical options include the maze procedure and AV node ablation with pacemaker implantation.¹

The maze procedure involves making a series of carefully-placed incisions in a tortuous maze-like path of atrial tissue, thereby directing impulses originating from the sinoatrial node across the atria into the AV node. The narrow path ensures that multiple reentry circuits cannot be sustained, thus preventing AF.¹

In the AV node ablation technique, high radio-frequency energy is applied to the AV junction, with the intention of producing an atrioventricular block and a slow escape rhythm from a junctional site.¹ A pacemaker can be implanted subsequently, to maintain an adequate heart rate.¹

Stroke Prevention (Anticoagulation)

Decisions on the need of anticoagulation treatment in patients with AF should be based on appropriate risk stratification for stroke. The CHADS2 (Cardiac Failure, Hypertension, Age, Diabetes, Stroke [Doubled]) is a com-

Table 2. Treatment options for acute and chronic AF¹

Chronic						
Acute			Chronic			
Rate Control			Rhythm Control			
Cardiac glycosides	Beta-blocker	Calcium channel blocker	Pharmacological – antiarrhythmic drugs		Electrical - Cardioversion	Surgical ablation
Digoxin	Metoprolol	Diltiazem	If <7 days, dofetilide, flecainide, ibutilide, propafenone	If >7 days, dofetilide, amiodarone, ibutilide, flecainide, propafenone, quinidine	*Defibrillation may increase risk of embolism by up to 2%; do TEE prior, to assess for atrial thrombus	1. MAZE procedure- series of incisions “maze-like” in atria 2. AV node ablation and pacemaker insertion

* TEE: transesophageal echocardiogram.

monly used tool to accomplish this. (Table 3). The score is formed by assigning 1 point each for the presence of CHF, hypertension, age greater than 75 years, and diabetes mellitus, and by assigning 2 points for a past history of stroke or transient ischemic attack.²¹ If the CHADS2 score is higher than or equal to 2 points, then warfarin is recommended.²¹

Table 3. Calculation for assessing the stroke risk for patients with AF using the CHADS2 score²¹

CHADS2 item	Points
CHF	1
Hypertension (sBP >160 mmHg)	1
Age > 75 years	1
Diabetes	1
Prior cerebral ischemia	2

Risks and Benefits of Anti-coagulation

The patients on warfarin for AF have a risk of major bleeding of approximately 2% per year.¹⁴ Major bleeding is defined as that which requires transfusion of at least two units of blood, and minor bleeding includes hematuria, epistaxis and GI bleeds that do not fit the criteria for major bleeding.¹⁴ Rates of minor bleeding were shown to be as high as 15.4% per year in patients on warfarin.¹⁴ Medical conditions that predispose patients to bleeding are hepatic or renal disease, diabetes, first AF episode, heart failure, and increased age.¹⁴

Table 4. A summary of recommended therapies for patients with AF based on their risk factors for thromboembolism

Antithrombotic Therapy for patients with atrial fibrillation ²⁴		
Less-validated/ weaker risk factors	Moderate risk factors	High risk factors
Female gender	Age ≥ 75 yr.	Previous stroke
Age 65-74 yr	Hypertension	Transient ischemic attack
Coronary artery disease	Heart Failure	Embolism
Thyrotoxicosis	Diabetes Mellitus	Mitral Stenosis
	Left v. ejection fraction < 35%	Prosthetic Heart Valve*
Risk Category	Therapy Recommended	
No risk factors	ASA 81-325mg daily	
1 moderate risk factor	ASA 81-325mg daily, or warfarin (INR 2.0-3.0, target 2.5)	
1+ moderate risk factor or any high risk factor	Warfarin (INR 2.0-3.9, target 2.5) *	

*If mechanical valve, target INR > 2.5

When the benefits of anticoagulation outweigh the risks, patients should be started on either unfractionated heparin (UFH) or low molecular weight heparin (LMWH) in the acute setting.¹⁴ Therapy is initiated with UFH or LMWH because of rapid onset of action, while maintenance therapy consists of warfarin. Warfarin takes several days to produce therapeutic anticoagulation as it works by inhibiting the production of vitamin K-dependent coagulation factors, and the existing coagu-

lation factors require several days to be depleted. However, warfarin has the immediate effect of inhibiting Protein C and Protein S, which are anticoagulants. Thus, warfarin induces a hypercoagulable state during the first three days of therapy.²² Therefore, warfarin and heparin should overlap for at least 4 to 5 days or until the INR value is within the therapeutic range for two consecutive days before heparin is discontinued.²³ The decision as to whether or not chronic anticoagulation therapy is needed in AF patients is based on risk stratification, as outlined in Table 4.

Aspirin has been shown to reduce the risk of strokes by approximately 20% (absolute risk reductions of 1.5% per year for primary prevention and 2.5% per year for secondary prevention.)²⁶ By contrast, adjusted-dose warfarin can reduce stroke risk by approximately 60%, with absolute risk reductions of 3% per year for primary prevention and 8% per year for secondary prevention.²⁶

Table 5. Characteristics of patients at high risk of bleeding while taking warfarin

- Age >75 years
- History of uncontrolled hypertension (defined as systolic blood pressure >180 mmHg or diastolic blood pressure >100 mmHg)
- Excess alcohol consumption (acute or chronic), liver disease
- Poor drug compliance or clinic attendance
- Bleeding lesions (especially gastrointestinal blood loss, such as peptic ulcer disease, or recent cerebral hemorrhage)
- Bleeding tendency (including coagulation defects, thrombocytopenia) or concomitant use of non-steroidal anti-inflammatory drugs or antibiotics
- Instability of INR control and INR >3

A recent meta-analysis found that treatment with warfarin is 40% more efficacious in preventing strokes than antiplatelet therapy. Even after accounting for risk of absolute increases in major extracranial hemorrhage, there were greater benefits of absolute reductions in stroke incidence.²⁷ Ultimately, it is only by considering the risks and benefits of treatment that a correct decision can be made for each individual patient.

CONCLUSION

Atrial fibrillation is the most common cardiac dysrhythmia.^{4,14} While its etiology is unclear, the condition is associated with aging, surgery, and various cardiac and non-cardiac diseases, including hypertension, cardiomyopathy, heart failure, PE, and thyrotoxicosis.

AF accounts for 25% of all strokes and doubles the mortality rate.^{4,25} This makes timely diagnosis and treatment imperative. In those suffering from AF and not treated with anticoagulation, the incidence of CVA averages approximately 5% per year, which can be decreased to 1% per year by managing AF with either rate or rhythm control.⁵

New-onset AF and chronic AF may be approached differently. If a patient with new-onset AF (less than 48 hours) is

hemodynamically unstable, then immediate electrical cardioversion is indicated. If a patient with chronic AF becomes hemodynamically unstable, then a TEE should be performed prior to electrical cardioversion to rule out potential atrial thrombus. The two main treatment strategies for hemodynamically stable patients with AF (both new onset and chronic) include rate control and rhythm control.^{4,15} Recent studies have shown that there is no significant difference in mortality rates between rate and rhythm control.^{4,15} However, rhythm control results in greater morbidity by increasing the risk of stroke at the time of spontaneous reversion to AF.¹⁴ Therefore, rate control is the treatment of choice.

Regardless of which treatment is used, anticoagulation therapy is currently recommended for stroke prevention, as the fibrillating heart has pockets of stasis leading to an increased risk of thrombus formation.^{28,29} Risk assessment can be done using the CHADS2 score, and this can guide the decision to proceed with anticoagulant therapy.¹⁹ As in many medical decisions, the benefits (prevention of strokes with anticoagulation therapy) should be weighed against the risks (induction of major and minor bleeding) but even so, warfarin therapy is indicated if the risk of a thromboembolic event is high. †

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