

Atrial Fibrillation: Goals of Therapy and Management Strategies to Achieve the Goals

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KEYWORDS

- Atrial fibrillation • Management • Rate control
- Rhythm control • Anticoagulation

Atrial fibrillation (AF) may be associated with disabling symptoms and complications, such as stroke and tachycardia-induced cardiomyopathy. Although AF, per se, is rarely a life-threatening arrhythmia, it was associated with decreased overall survival in the Framingham Heart Study.¹ The three major therapeutic strategies in managing AF include prevention of stroke, rate control, and rhythm control. Anticoagulation with warfarin reduces the risk for stroke. Therapies to achieve symptom control and prevention of tachycardia-mediated cardiomyopathy are often similar. For example, ventricular rate control during AF or maintenance of sinus rhythm may improve symptoms and prevent tachycardia-induced cardiomyopathy. When clinical goals are not met using one strategy, the alternate strategy can be pursued in the same patient. Current therapies of AF have not demonstrated survival benefits, and future research needs to focus on the goals of improving the survival of patients who have AF. Development of strategies for the primary prevention of AF is another area of great significance for research considering the high prevalence of the disease. Until such therapeutic options become available, prevention of the disease-related complications and control of symptoms may be considered the primary goals of AF management (**Box 1**).

GOALS OF THERAPY

Prevention of Thromboembolism

AF, with its accompanying loss of organized atrial contraction, can lead to stagnation of blood, especially in the left atrial appendage, with resultant thrombus formation and embolism. There is also some evidence that AF is associated with a hypercoagulable state, further promoting thromboembolism.^{2,3} Stroke, the most common thromboembolic event in AF, occurs at a higher frequency in individuals who have AF, and approximately 36% of all strokes in individuals aged 80 to 89 years are attributed to AF.⁴ Furthermore, strokes occurring in patients who have AF tend to have a higher degree of severity.⁵ Individuals who have AF are not at equal risk for thromboembolic events, and several predisposing clinical factors can identify those patients at high risk. Anticoagulation with warfarin is the current standard of therapy for preventing thromboembolism in patients at high risk for stroke. The goal of anticoagulation is to prevent AF-related thromboembolic complications without increasing the risks for bleeding significantly. There is evidence that suggests warfarin therapy is underused in patients who have AF;^{6,7} more widespread use of warfarin therapy in appropriate patients is another goal to be achieved. An important lesson learned from recent clinical trials of AF management is that

A version of this article originally appeared in *Medical Clinics of North America*, volume 92, issue 1. The Care Group, LLC, 8333 Naab Road, Suite 400, Indianapolis, IN 46260-1919, USA

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Cardiol Clin 27 (2009) 189–200

doi:10.1016/j.ccl.2008.09.006

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Box 1**Goals of atrial fibrillation therapy**

Prevention of stroke (thromboembolism)

Prevention of tachycardia-induced cardiomyopathy

Symptom relief

Improved survival

Primary prevention

patients at high risk for stroke who seem to be maintaining sinus rhythm while receiving antiarrhythmic medications still require warfarin therapy.^{8,9} These patients have a continued risk for stroke, possibly from clinically unrecognized episodes of AF.

Prevention of Tachycardia-Induced Cardiomyopathy

Untreated AF often is associated with rapid ventricular rates. In experimental models, ventricular dysfunction can occur as soon as 24 hours and continue to deteriorate for 3 to 5 weeks with rapid pacing rates. Recovery of ventricular function with cessation of pacing could start within 48 hours, and normalization can occur within 1 to 2 weeks.¹⁰ Patients who have AF and prolonged periods of rapid ventricular rates may develop left ventricular (LV) dysfunction, although the severity and temporal course of its onset vary significantly among individuals. In a study of AV node ablation and permanent pacemaker placement for AF refractory to medical therapy, 37% (105 of 282) of patients had an LV ejection fraction of 40% or less,¹¹ indicating a high prevalence of cardiomyopathy in such patients. Control of ventricular rates, by rate or rhythm control strategies, when undertaken early after AF onset, can prevent subsequent development of cardiomyopathy. If patients already have developed tachycardia-induced ventricular dysfunction at presentation, the immediate goal is to reverse this process with aggressive rate control or cardioversion to sinus rhythm. In such patients, particular attention should be paid to avoid recurrent AF with prolonged periods of rapid ventricular rates, because rather quick development of LV failure and incidents of sudden death are reported in the literature with recurrent tachycardia-induced cardiomyopathy.¹²

Control of Symptoms

Patients who have AF exhibit a panoply of clinical presentations, ranging from none to disabling symptoms. Common symptoms include anxiety,

palpitations, dyspnea, dizziness, chest pain, and fatigue. Several hemodynamic derangements, including rapid ventricular rates, loss of organized atrial contraction, irregularity of cardiac rhythm, and bradycardia (resulting particularly from sinus pauses when AF episodes terminate), may be the underlying cause of the symptoms related to AF. Although the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial⁸ demonstrated that symptoms can be controlled equally well with a rate control or rhythm control strategy, clinicians encounter many patients who have AF who need sinus rhythm to feel better. This may be particularly relevant in younger patients and those who have paroxysmal AF. The loss of regularity and fine autonomic control of cardiac rhythm and the loss of atrial contribution to ventricular filling may be postulated as playing a bigger role in the hemodynamics of these patients, accounting for the lack of success of rate control. When a rate control strategy is selected, it is important to allow adequate time for symptoms to improve, because in many patients, it can take several months for good symptom relief after achieving rate control. Control of symptoms rather than elimination of all symptoms may be an acceptable goal in many patients based on a risks/benefits analysis of the available therapeutic options.

Future Goals

Improvement in survival should be a goal of AF therapy. Elucidation of basic mechanisms of the disease and targeted therapy that does not have significant adverse effects (eg, atrial-specific antiarrhythmic drugs),¹³ continued anticoagulation in patients taking antiarrhythmic drugs for rhythm control,¹⁴ and catheter ablation strategies to cure AF could potentially improve patient survival. Preliminary data comparing ablation with antiarrhythmic medications show favorable outcomes for the ablation strategy.^{15,16}

Primary prevention of AF is an important public health goal because it affects an estimated 2.2 million people in the United States¹⁷ and its prevalence is rising.¹⁸ Preliminary data suggest that the use of medications, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors in addition to dietary intake of fish and n-3 polyunsaturated fatty acids may reduce AF incidence.¹³ Whether or not treatment of disease states, such as hypertension and heart failure, that have a known association with AF could lead to a decreased incidence of AF also needs evaluation.

THERAPEUTIC OPTIONS

Anticoagulation

Risk stratification

Because anticoagulation therapy is inherently associated with an increased risk for bleeding complications, such therapy is limited to patients who have AF and are deemed to be at high risk for thromboembolism. Collective information from various clinical trials of anticoagulation therapy has identified several risk factors that predispose persons who have AF to thromboembolism.¹⁹ Gage and colleagues²⁰ developed a scoring system for stroke risk prediction called CHADS2 using these risk factors. Each of the letters in this acronym represents a risk factor—congestive heart failure, hypertension, age, diabetes, and stroke. Previous stroke or transient ischemic attack (TIA) is the strongest predictor of stroke, and therefore carries two points, whereas the other risk factors carry one point each. The American College of Cardiology (ACC)/American Heart Association (AHA)/European Society of Cardiology (ESC) guidelines on AF management use the CHADS2 scoring for risk classification.²¹ **Box 2** summarizes the ACC/AHA/ESC system of dividing predisposing factors into less validated or weaker risk factors, moderate risk factors, and high risk factors. Patients who have any high risk factor or more than one moderate risk factor are considered at high risk (>4% annual risk) for stroke, and warfarin is recommended. Those who have no risk factors are considered at low risk (<2% annual risk) for stroke and are generally prescribed aspirin

Box 2

Risk factors for thromboembolism

Less validated risk

Female gender
Age 65 to 74 years
Coronary artery disease
Thyrototoxicosis

Moderate risk

Age 75 years or older
Hypertension
LV ejection fraction 35% or less
Heart failure
Diabetes mellitus

High risk

Previous stroke, TIA, embolism
Mitral stenosis
Prosthetic heart valve

Box 3

Risk category and recommended therapy

No risk factors: aspirin (81 mg/d or 325 mg/d)
One moderate risk factor: aspirin or warfarin
Any high risk factor or more than one moderate risk factor: warfarin

(Box 3). Patients who have one moderate risk factor have an intermediate risk (2.8% annual risk) for stroke.^{20,21} Treatment decisions are individualized in these latter patients, and warfarin or aspirin may be used.²¹

Warfarin

Warfarin therapy is highly effective, compared with placebo, in reducing (by 61%) the stroke risk in patients who have AF.²² Strokes occurring in patients who have AF while they are taking warfarin therapy also are less severe.²³ In clinical studies, an international normalized ratio (INR) between 2.0 and 3.0 correlates to maximum protection against strokes with minimum bleeding risks.²⁴ Warfarin has several drawbacks, including a 1% to 1.5% risk for major bleeding complications.¹⁹ The risk for bleeding may be higher in women and in the elderly, who also are at the highest risk for embolic stroke from AF.^{25,26} The risk for bleeding seems higher at initiation of warfarin, and a recent study has noted a threefold increase in bleeding risk during the first 3 months of therapy.²⁷

Alternatives to warfarin

Aspirin is significantly less effective than warfarin, with a stroke reduction of only 19%.²² Aspirin, however, is recommended in lower risk patients because of its favorable side-effect profile and ease of use. In a clinical study of high-risk patients, a combination of aspirin and clopidogrel was inferior to warfarin for stroke prevention.²⁸ Ximelagatran (an oral direct thrombin inhibitor) did not meet US Food and Drug Administration approval because of concerns regarding its hepatotoxicity and clinical trial design.²⁹ Nonpharmacologic stroke prevention, a consideration only in high-risk patients who are not candidates for warfarin, has not been well studied. Approaches include surgical left atrial appendage removal and catheter-based left atrial appendage occlusion.^{30,31}

Anticoagulation management before cardioversion

The use of anticoagulation before and after cardioversion (electrical or pharmacologic) requires special consideration because of increased risk for stroke noted in retrospective studies after

cardioversion.³² According to the current guidelines,²¹ patients may be cardioverted without anticoagulation if the duration of AF is less than 48 hours. When the duration of AF is unknown or greater than 48 hours, anticoagulation with warfarin should be instituted with a therapeutic INR for at least 3 weeks before and 4 weeks after the cardioversion.²¹ An alternative approach is a transeophageal echocardiogram to exclude the presence of left atrial thrombus,³³ followed by cardioversion. In this approach, it is not necessary to have 3 weeks of therapeutic INR before the cardioversion and patients who do not have a therapeutic INR may be given intravenous unfractionated heparin or subcutaneous low-molecular-weight heparin to achieve immediate anticoagulation.^{33,34} Cardioversion, however, should be followed by continued unfractionated or low-molecular-weight heparin therapy until the INR is therapeutic, and warfarin should be continued for at least 4 weeks.

Rate Control and Rhythm Control

The two basic therapeutic options to control symptoms in AF are rhythm control, in which sinus rhythm is re-established, and rate control, in which patients remain in AF with control of ventricular rates. Pharmacologic and nonpharmacologic options are available for both of these strategies.

Although re-establishing the normal rhythm (the rhythm control strategy) may seem to be intuitively superior, clinical studies show no significant difference in major clinical outcomes between this strategy and that of rate control. Five randomized clinical trials looked at total mortality, thromboembolic events, hemorrhage, and symptomatic improvement and found no statistically significant differences in outcomes between the pharmacologic rate control and rhythm control strategies.^{8,9,35–37} The mean age of participants in the largest of these trials (AFFIRM) was 69.7 years, leading many clinicians to choose rate control as a preferred strategy in older less symptomatic patients.

The reasons for the lack of advantage of sinus rhythm maintenance in clinical trials are not clear but could relate to the toxicity associated with antiarrhythmic medications, negating the advantages of sinus rhythm. Another important factor may be the discontinuation of anticoagulation in patients, seemingly maintaining sinus rhythm in such trials. In fact, one of the important messages from rate control versus rhythm control trials is the need for continued anticoagulation therapy in high-risk patients while they are clinically maintaining sinus rhythm on antiarrhythmic medications. Preliminary evidence suggesting that the toxicity

of current antiarrhythmic medications may negate the advantages of sinus rhythm is as follows. A retrospective subanalysis of the on-treatment outcomes in the AFFIRM study suggests that a strategy to maintain sinus rhythm without the adverse effects of antiarrhythmic medications may confer a survival advantage.¹⁴ Radiofrequency ablation trials also shed some light on this debate. In a nonrandomized study, Pappone and colleagues¹⁵ compared the outcomes in a selected group of 589 patients who underwent circumferential pulmonary vein ablation with those in 582 age- and gender-matched cohort patients who received antiarrhythmic medications to maintain sinus rhythm. After a median follow-up of 900 days, the observed survival was longer and the quality of life was better for patients who underwent ablation. Radiofrequency pulmonary vein isolation was a superior first-line therapy compared with antiarrhythmic drug therapy in a small randomized trial of 70 patients.¹⁶ Finally, in patients who had heart failure, ablation resulted in improved heart function even when heart rates were well controlled before ablation.^{38,39} Thus, future use of antiarrhythmic medications with a better side-effect profile and advancements in ablation techniques could lead to better outcomes with rhythm control strategy.

Choice of strategy

The choice of a particular strategy should be dictated by the clinical scenario, with a preference toward rate control in less symptomatic elderly patients. Rate control also may be preferred in patients who are noncompliant or decline hospitalization and cardioversion, because the rhythm control strategy may require a higher number of hospitalizations.⁸ Patients in whom the only antiarrhythmic choice is amiodarone also are potential candidates for an initial rate control strategy. An initial rhythm control strategy may be appropriate in younger symptomatic patients, newly diagnosed patients who have lone AF, and those who have AF believed to be secondary to a precipitating event. Although a retrospective analysis suggested improved survival by maintaining sinus rhythm in patients who had heart failure,^{8,40,41} results of the recent randomized prospective trial of 1376 patients who had heart failure and a left ventricular ejection fraction (LVEF) less than 35% showed no significant differences in outcomes between a rhythm control and rate control strategy.⁴²

Definition of rate control

The best parameters for rate control in AF are not well defined, but the AFFIRM study criteria generally are recommended^{8,21} (ventricular rate ≤ 80

beats per minute at rest and a maximum of <110 beats per minute during a 6-minute walk or an average heart rate <100 beats per minute during 24-hour ambulatory monitoring with no heart rate >110% of the maximal age-predicted exercise heart rate). It is unclear whether or not strict heart rate control is essential for good outcomes, especially in patients who do not have LV dysfunction and significant symptoms. Cooper and colleagues⁴³ analyzed the outcomes in different quartiles of heart rate control in the AFFIRM study (heart rate quartiles at rest: 44–69, 70–78, 79–87, and 88–148 beats per minute and heart rate quartiles with a 6-minute walk: 53–82, 83–92, 93–106 and 107–220 beats per minute) and found no differences in overall survival or quality of life. These data may indicate that strict heart rate control may not be essential for good outcomes in some patients. At the authors' institution, physicians prefer to regulate the heart rate for AF in each patient's normal daily activity profile. To accomplish this, the daily heart rate trend graphs from 24-hour electrocardiographic (ECG) recordings are used and medications are adjusted to maintain average rates for each hour of less than 100 beats per minute and for a 24-hour period of approximately 70 to 80 beats per minute.⁴⁴

Therapeutic options for rate control

Beta-blockers, nondihydropyridine calcium channel blockers, and digoxin are the usual pharmacologic agents used for rate control. Digoxin is less effective than beta-blockers and calcium channel blockers, particularly during exercise, but has a synergistic effect when added to them.⁴⁵ Beta-blockers are preferred as an initial AV blocking agent when there is LV dysfunction associated with AF.^{46,47} Calcium channel blockers, verapamil and diltiazem in a sustained released form, often are well tolerated by patients who have bronchospastic disease. At times, it is useful to give smaller doses of two classes of drugs to minimize adverse effects. Amiodarone and clonidine also have been used for rate control purposes in limited situations.^{21,48} AV junction ablation with permanent pacemaker implantation (ablate and pace strategy) is a highly effective method for rate control but is usually reserved for situations in which pharmacologic options are ineffective. Clinical studies have demonstrated improvement in quality of life and LV function with such an approach.^{49,50} Concerns with this approach include patients becoming pacemaker dependent, provocation of fatal ventricular arrhythmias, and the more recently described deleterious effects of permanent right ventricular pacing.⁵¹ Consideration may be given to biventricular pacing for patients who have

significant LV dysfunction undergoing AV junction ablation for AF rate control to address the potential deleterious effects of right ventricular pacing in that situation.^{52–54}

Rhythm control with antiarrhythmic medications

Antiarrhythmic medications, by changing the electrophysiologic properties of atrial tissue, can terminate AF or prevent its recurrence. The Vaughan-Williams classification divides these agents into class IA, IB, and IC (sodium channel blockers); class II (beta-blockers); class III (potassium channel blockers); and class IV (calcium channel blockers). Only class I and class III agents are referred to as antiarrhythmic medications in this article because beta-blockers and calcium channel blockers do not have the ability to cardiovert AF or maintain sinus rhythm after cardioversion of AF.

Choice of antiarrhythmic medication

Selection of antiarrhythmic agents should be directed by a safety-based approach (**Fig. 1**). The class IC agent flecainide increased mortality in the setting of previous myocardial infarction and ventricular ectopy in the Cardiac Arrhythmia Suppression Trial.⁵⁵ Based on this information, the class IC agents flecainide and propafenone are considered to be contraindicated in patients who have AF with ischemic heart disease.²¹ Class IC agents do not increase mortality in patients who have structurally normal hearts,⁵⁶ however, making them one of the initial agents of choice for treatment of AF. Class III (sotalol and dofetilide) and class IA (quinidine, procainamide, and disopyramide) agents prolong cardiac repolarization, and therefore can be associated with the torsades de pointes form of ventricular tachycardia. Although many patients at risk can be identified by monitoring for early proarrhythmia and QT prolongation on ECG, late episodes of torsades de pointes can occur, particularly in the setting of hypokalemia, bradycardia, or renal dysfunction.⁵⁷ Amiodarone is a multi-ion channel-blocking agent (included in class III) and prolongs QT interval but has a low risk for causing torsades de pointes. Amiodarone is the most effective antiarrhythmic drug available, and in the Canadian Trial of Atrial Fibrillation, only 35% of patients taking amiodarone had recurrent AF compared with 63% of those taking propafenone or sotalol during a mean follow-up of 468 (± 150) days.⁵⁸ Amiodarone, however, has many organ toxicities—thyroid, pulmonary, neurologic, hepatic, optic neuropathy (rare), and dermatologic effects⁵⁹—that limit its usefulness. In a meta-analysis of 44 antiarrhythmic

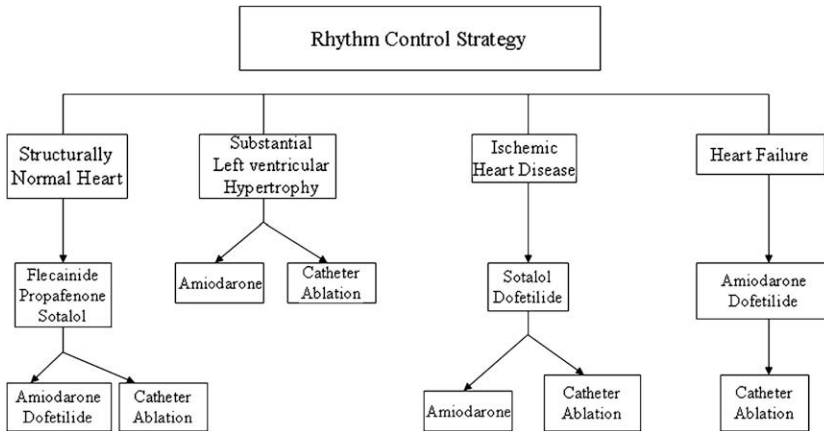


Fig. 1. Approach to selection of therapy to re-establish sinus rhythm in patients who have AF.

medication trials (11,322 patients), sotalol, dofetilide, or amiodarone did not show any significant change in mortality compared with placebo, and the same review showed increased mortality associated with the use of class IA drugs compared with placebo.⁵⁶

When selecting an antiarrhythmic medication for AF treatment, first determine if the heart structurally is normal. The initial choice of an antiarrhythmic medication in patients who have structurally normal hearts and normal 12-lead ECGs is flecainide, propafenone, or sotalol. In the presence of LV hypertrophy (>1.4 cm), amiodarone is the preferred initial therapy because of the perceived potential for proarrhythmia with other agents.²¹ Only amiodarone and dofetilide are demonstrated not to decrease survival in the setting of heart failure, making them the preferred agents for these patients. Patients who have ischemic heart disease usually are given sotalol or dofetilide as an initial agent. Sotalol and dofetilide are excreted through the kidneys and should be avoided in patients who have significant renal dysfunction. Bradycardia accentuates QT prolonging effects of sotalol and dofetilide, and patients may require permanent pacing to facilitate the use of these agents in this scenario. Finally, consider avoiding these latter medications in patients who have complex medical regimens, particularly if significant variations in serum electrolytes could occur.

Outpatient initiation of antiarrhythmic medications

Dofetilide therapy always is initiated in a hospital with daily 12-lead ECGs and telemetry monitoring for at least 3 days. All other antiarrhythmic medications can be initiated in an outpatient setting in patients who have no or minimal heart disease per current guidelines.²¹ In the presence of heart

disease, the authors recommend starting sotalol during constant heart rhythm monitoring in a hospital. Patients who are in AF at the time of therapy initiation also are candidates for inpatient treatment because they may have unidentified sinus node dysfunction, leading to significant bradycardia with conversion of AF to sinus rhythm. One exception is amiodarone initiation at low doses of 200 to 600 mg/d. Here, drug loading takes several weeks, and it is impractical to monitor patients in the hospital. When drugs are initiated on an outpatient basis, the authors recommend 12-lead ECGs 2 to 3 days after each dose change. ECGs are analyzed for excessive prolongation of the QT interval (corrected QT interval [QT_c] >500 milliseconds) with sotalol and for prolongation of the PR interval and QRS duration with flecainide or propafenone.

Cardioversion

Conversion of AF to sinus rhythm can be done using synchronized external shocks or antiarrhythmic medications at loading doses. Anticoagulation issues must be addressed before pharmacologic or electrical cardioversions. AF, unlike atrial flutter, is not a rhythm that can be terminated with overdrive pacing. A "pill-in-the-pocket" strategy of outpatient cardioversion may be attempted using loading doses of propafenone or flecainide in some patients.⁶⁰ The first such attempt, however, should be done in a hospital setting²¹ to establish safety. Administration of beta-blockers or calcium channel blockers is recommended at least 30 minutes before administration of high-dose propafenone or flecainide to prevent development of atrial flutter with 1:1 atrioventricular conduction leading to potentially life-threatening ventricular rates.²¹

Nonpharmacologic rhythm control

When rhythm maintenance is needed and antiarrhythmic medications are ineffective, radiofrequency catheter ablation approaches may be considered. Recent observations from Haissaguerre and colleagues^{61,62} have demonstrated that the initiators of AF typically originate in the pulmonary veins and that electrical isolation of these veins often prevents AF. Many different ablation techniques subsequently have been described, and the best AF ablation technique to eliminate AF in individual patients has yet to be defined.⁶³ The surgical maze procedure to cure AF is highly effective, but this is typically reserved for patients who have failed the catheter ablation approach or for patients undergoing another open-heart procedure, when it is added onto the primary procedure.⁶⁴

MANAGEMENT STRATEGIES BASED ON CLINICAL PRESENTATIONS

Initial Approach to any Patients who Have Atrial Fibrillation

History, physical examination, and laboratory tests

Initial evaluation of AF should include a clinical history regarding the time of onset and the nature of patient's symptoms (Fig. 2). Attention should be directed to identifying a possible precipitating event that led to AF. Symptoms suggestive of complications, such as heart failure and stroke, also should be part of the history. Physical examination is directed to vital signs and cardiovascular and other system examinations, especially to increase the information obtained from the history. Initial laboratory testing should include a complete blood cell count, a metabolic panel, and renal and thyroid function evaluations. A two-dimensional echocardiogram is indicated in most patients to identify causative factors for AF and to evaluate for LV dysfunction.

Hemodynamics

Initial attention is directed to the hemodynamic stability of patients. AF, particularly with rapid ventricular rates, can result in severe hemodynamic compromise, especially in patients who have heart disease in which cardiac output is heavily dependent on the atrial contribution and diastolic filling time of the ventricle. Examples include hypertrophic cardiomyopathy with its associated noncompliant ventricles, diastolic dysfunction, and severe mitral stenosis. Significant hemodynamic instability also can occur in scenarios in which there is preexisting hemodynamic compromise, such as sepsis, myocardial infarction, or pulmonary

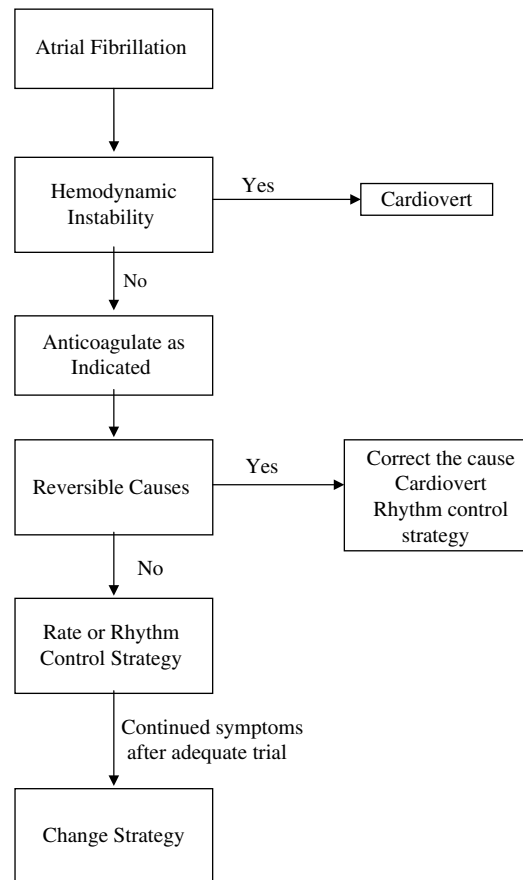


Fig. 2. General approach to patients presenting with AF.

embolism. Patients who have life-threatening hemodynamic compromise need emergent cardioversion without consideration of anticoagulation status. These patients also are at risk for recurrent AF after the cardioversion and may need treatment with intravenous antiarrhythmic drugs, such as amiodarone, to maintain sinus rhythm or to control ventricular rates during AF. Digoxin is another agent that can provide rate control without causing hypotension; however, its effectiveness is minimized in these states of high sympathetic tone.

Precipitating factors

Once the hemodynamic status is addressed, potential precipitating events that caused AF are evaluated. Examples of cardiac disorders that may underlie AF include pericarditis, heart failure, thoracic surgery, Wolff-Parkinson-White syndrome, and mitral stenosis. Several noncardiac conditions also can precipitate AF, for example, pneumonia, pulmonary embolism, acute hypoxia, thyrotoxicosis, and alcohol binge drinking. Although AF may not recur when precipitating

factors are eliminated, there is a distinct possibility that AF episodes may continue to occur and that the correlation was coincidental or the precipitating event simply brought out the underlying causative AF pathophysiology. Therefore, AF in patients who have possible precipitating events is initially managed the same way as is AF in other patients with regard to anticoagulation. Anticoagulation should be considered in all high-risk patients with the understanding that it can be discontinued if there are no clinical AF recurrences during follow-up. For moderate-risk patients in whom warfarin anticoagulation is optional, waiting to see if AF recurs in the absence of the initial precipitating event before initiating anticoagulation treatment is reasonable. A rhythm control rather than a rate control approach is preferred because of the distinct possibility of long-term sinus rhythm maintenance without antiarrhythmic medications. Short-term antiarrhythmic therapy may be considered if the initial AF episode is persistent.

Newly Diagnosed Atrial Fibrillation

Persistent atrial fibrillation

In patients presenting with new-onset symptoms, it may be worth waiting at least 24 hours to determine if the AF self-terminates. At least one attempt at establishing sinus rhythm is reasonable in most patients who have a new diagnosis of AF, because some patients may maintain sinus rhythm for prolonged periods after an initial cardioversion. Older asymptomatic patients who have no precipitating events for AF may be managed with rate control from the beginning. When AF is diagnosed for the first time in a patient, the time of onset of the arrhythmia may or may not be clear based on clinical history. Because it has an impact on anticoagulation decisions for cardioversion, meticulous attention should be paid to establish the time at which AF started. A history of palpitations and dyspnea is unreliable, particularly in elderly patients, and these may signify AF-related heart failure symptoms rather than the onset of the arrhythmia itself. It may be wise to err on the side of indeterminate time of onset in elderly patients and patients who have multiple stroke risk factors and have the patients undergo 3 weeks of anticoagulation or a transesophageal echocardiogram before cardioversion. If the time of onset is clear and less than 48 hours based on the history, particularly in young patients, cardioversion (electrical or pharmacologic) may be considered without anticoagulation.

Paroxysmal atrial fibrillation

Because AF episodes are self-terminating, cardioversion is unnecessary. Antiarrhythmic

medications should be avoided until a pattern of recurrent symptomatic episodes is established. Rate control may be needed and should be guided by symptoms. Patients who have minimally symptomatic and infrequent episodes may not need any treatment other than anticoagulation considerations.

Recurrent Atrial Fibrillation

In most patients, persistent or paroxysmal AF recurs after the initial event. Anticoagulation decisions are made based on the risk profile for stroke and are not affected by the persistent or paroxysmal nature of AF. The decision of pursuing a rhythm or rate control strategy depends on individual patient factors. In general, based on general principles (as discussed previously), rate control is favored in older less symptomatic patients. For patients who have infrequent but highly symptomatic persistent AF episodes, a pill-in-the-pocket strategy may be appropriate and can help to reduce the risk for side effects related to long-term antiarrhythmic therapy. Catheter ablation is an option for persistent and paroxysmal AF when antiarrhythmic therapy is ineffective in controlling symptoms.

Permanent Atrial Fibrillation

Permanent atrial fibrillation is a term applied to cases in which patients are allowed to remain in AF without further attempts at rhythm control, because rhythm control is deemed unnecessary or not attainable with a reasonable risk/benefit ratio. Anticoagulation should be administered when indicated based on risk factors. Ventricular rate control must be addressed in all cases.

Tachycardia-Bradycardia Syndrome

Patients who have paroxysmal AF may have high ventricular rates during AF episodes and bradycardia during sinus rhythm. Similarly, patients who have persistent or permanent AF may present with uncontrolled high ventricular rates at times and symptomatic slow ventricular rates at other times. These two situations, in which tachycardia and bradycardia are present in the same patient, present a scenario in which rate control and antiarrhythmic medications are difficult to use. Permanent pacemaker implantation usually is necessary to facilitate appropriate therapy. Sinus node dysfunction may resolve after a successful catheter ablation of AF and may be a consideration, particularly in young patients, to avoid the need for permanent pacing.⁶⁵

Atrial Fibrillation with Heart Failure

Patients presenting with heart failure (systolic or diastolic dysfunction) resulting from AF generally have high ventricular rates. Cardioversion to sinus rhythm and initiation of an antiarrhythmic medication (dofetilide or amiodarone) usually are needed, because such patients often do not tolerate beta-blockers or calcium channel blockers for rate control. The need for cardioversion is less clear when ventricular rates are controlled at presentation.

Postoperative Atrial Fibrillation

AF occurs in approximately one third of patients after open heart surgery.⁶⁶ It is an important risk factor for postoperative stroke, and anticoagulation should be instituted despite the increased bleeding risk inherent in this setting.^{66–68} A meta-analysis of 42 clinical trials showed benefits of beta-blockers, sotalol, and amiodarone in reducing the incidence of postoperative AF.⁶⁹ Beta-blockers are recommended routinely for patients undergoing cardiac surgery, and amiodarone may be considered for patients at high risk for postoperative AF.²¹

Atrial Fibrillation and Wolff-Parkinson-White Syndrome

Wolff-Parkinson-White syndrome presents two specific clinical problems with AF. First, an accessory pathway-mediated atrioventricular reentry tachycardia can degenerate into AF. Second, in some patients who have accessory pathways capable of rapid conduction to the ventricle, the AF may degenerate into ventricular fibrillation and cause sudden death.⁷⁰ Electrical cardioversion is necessary if patients are hemodynamically unstable. In stable patients, intravenous procainamide or amiodarone can be used to slow conduction over the accessory pathway. Intravenous beta-blockers and calcium channel blockers could result in hypotension and accelerated conduction over the accessory pathway and are contraindicated in this setting. Digoxin also is contraindicated in this setting because of concerns of accelerated conduction over the accessory pathway and the paradoxical effect of increased ventricular rates from AV node blockade.²¹ Definitive therapy is radiofrequency ablation of the accessory pathway.

SUMMARY

The primary goals in the management of patients who have AF are the prevention of stroke and cardiomyopathy and the amelioration of symptoms.

Each patient presents to a physician with a specific constellation of symptoms and signs, but, fortunately, most patients can be assigned to broad categories of therapy. For some, anticoagulation and rate control suffice, whereas others require more aggressive attempts to restore and maintain sinus rhythm. Physicians and patients need to be willing to alter therapeutic plans if an initial strategy of rate or rhythm control is unsuccessful.

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