ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation: Executive Summary

A Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation)

Developed in Collaboration With the North American Society of Pacing and Electrophysiology

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I. Introduction

Atrial fibrillation (AF), the most common sustained cardiac rhythm disturbance, is increasing in prevalence as the population ages. Although it is often associated with heart disease, AF occurs in many patients with no detectable disease. Hemodynamic impairment and thromboembolic events result

This document was approved by the American College of Cardiology Board of Trustees in August 2001, the American Heart Association Science Advisory and Coordinating Committee in August 2001, and the European Society of Cardiology Board and Committee for Practice Guidelines and Policy Conferences in August 2001.

When citing this document, the American College of Cardiology, the American Heart Association, and the European Society of Cardiology would appreciate the following citation format: Fuster V, Rydén LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, Halperin JL, Kay GN, Klein WW, Lévy S, McNamara RL, Prystowsky EN, Wann LS, Wyse DG. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation). *Circulation*. 2001;104:2118–2150.

This statement has been co-published in the October 2001 issue of the *Journal of the American College of Cardiology*.

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(*Circulation* 2001;104:2118–2150.)

in significant morbidity, mortality, and cost. Accordingly, the American College of Cardiology (ACC), the American Heart Association (AHA), and the European Society of Cardiology (ESC) created a committee of experts to establish guidelines for management of this arrhythmia.

The committee was composed of 8 members representing the ACC and AHA, 4 representing the ESC, 1 from the North American Society of Pacing and Electrophysiology (NASPE), and a representative of the Johns Hopkins University Evidence-Based Practice Center representing the Agency for Healthcare Research and Quality's report on Atrial Fibrillation in the Elderly. This document was reviewed by 3 official reviewers nominated by the ACC, 3 nominated by the AHA, and 3 nominated by the ESC, as well as by the ACC Clinical Electrophysiology Committee, the AHA ECG and Arrhythmia Committee, NASPE, and 25 reviewers nominated by the writing committee. The document was approved for publication by the governing bodies of the ACC, AHA, and ESC and officially endorsed by NASPE. These guidelines will be reviewed annually by the task force and will be considered current unless the task force revises or withdraws them from distribution.

The committee conducted a comprehensive review of the literature from 1980 to June 2000 relevant to AF using the following databases: PubMed/Medline, EMBASE, the Cochrane Library (including the Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Registry), and Best Evidence. Searches were limited to English language sources and to human subjects.

II. Definitions

A. Atrial Fibrillation

AF is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation with consequent deterioration of atrial mechanical function. On the electrocardiogram (ECG), AF is described by the replacement of consistent P waves by rapid oscillations or fibrillatory waves that vary in size, shape, and timing, associated with an irregular, frequently rapid ventricular response when atrioventricular (AV) conduction is intact (1). The ventricular response to AF depends on electrophysiological properties of the AV node, the level of vagal and sympathetic tone, and the action of drugs (2). Regular RR intervals are possible in the presence of AV block or interference by ventricular or junctional tachycardia. A rapid, irregular, sustained, wide-QRS-complex tachycardia strongly suggests AF with conduction over an accessory pathway or AF with underlying bundle-branch block. Extremely rapid rates (over 200 bpm) suggest the presence of an accessory pathway.

B. Related Arrhythmias

AF can be isolated or associated with other arrhythmias, often atrial flutter or atrial tachycardia. Atrial flutter can arise during treatment with antiarrhythmic agents prescribed to prevent recurrent AF. Atrial flutter is more organized than AF, with a saw-tooth pattern of regular atrial activation called flutter (f) waves on the ECG, particularly visible in leads II, III, and aVF. Untreated, the atrial rate typically ranges from 240 to 320 beats per minute (bpm), with f waves inverted in ECG leads II, III, and aVF and upright in lead V_1. The wave of activation in the right atrium (RA) may be reversed, resulting in f waves that are upright in leads II, III, and aVF and inverted in lead V_1. Two-to-one AV block is common, producing a ventricular rate of 120 to 160 bpm. Atrial flutter can degenerate into AF, AF can initiate atrial flutter, or the ECG pattern can alternate between atrial flutter and AF, reflecting changing atrial activation.

Other atrial tachycardias, as well as AV reentrant tachycardias and AV nodal reentrant tachycardias, can also trigger AF. In other atrial tachycardias, P waves are readily identified and are separated by an isoelectric baseline in 1 or more ECG leads. The morphology of the P waves can help localize the origin of atrial tachycardias. A unique type of atrial tachycardia originates in the pulmonary veins (3), is typically more rapid than 250 bpm, and often degenerates into AF. Intracardiac mapping can help differentiate the various atrial arrhythmias.

III. Classification

AF has a heterogeneous clinical presentation, occurring in the presence or absence of detectable heart disease or related symptoms. For example, the term "lone AF" has been variously defined. The prognosis in terms of thromboembolism and mortality is most benign when applied to young individuals (aged less than 60 years) without clinical or echocardiographic evidence of cardiopulmonary disease (4). These patients have a favorable prognosis with respect to thromboembolism and mortality. By virtue of aging or the development of cardiac abnormalities, however, patients move out of the lone AF category over time, and the risks of thromboembolism and mortality rise. Lone AF is distinguished from idiopathic AF, which implies uncertainty about its origin without reference to the age of the patient or associated cardiovascular pathology. By convention, the term nonvalvular AF is restricted to cases in which the rhythm disturbance occurs in the absence of rheumatic mitral stenosis or a prosthetic heart valve.

The classification scheme recommended in this document represents a consensus driven by a desire for simplicity and clinical relevance. The clinician should distinguish a first-detected episode of AF, whether or not it is symptomatic or self-limited, recognizing that there can be uncertainty about the duration of the episode and about previous undetected episodes (Fig. 1). When a patient has had 2 or more episodes, AF is considered recurrent. Once terminated, recurrent AF is designated paroxysmal, and when sustained, persistent. In the latter case, termination by pharmacological therapy or electrical cardioversion does not change the designation. Persistent AF can be either the first presentation or a culmination of recurrent episodes of paroxysmal AF. Persistent AF includes cases of long-standing AF (eg, greater than 1 year), in which cardioversion has not been indicated or attempted, usually leading to permanent AF (Fig. 1). The terminology defined in the preceding paragraph applies to episodes of AF that last more than 30 seconds and that are unrelated to a reversible cause. AF secondary to a precipitating condition such as acute myocardial infarction, cardiac surgery, myocarditis, hyperthyroidism, or acute pulmonary disease is considered separately. In these settings, treatment of the underlying disorder

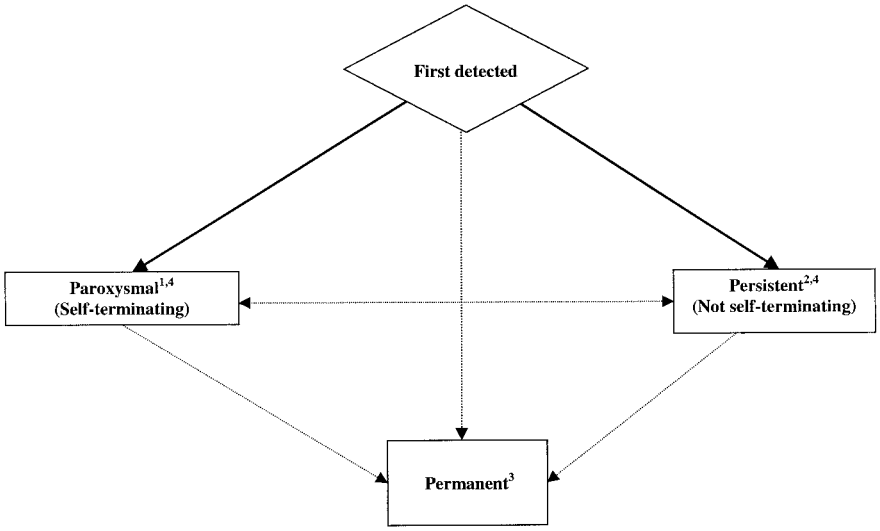

Figure 1. Patterns of atrial fibrillation. 1, episodes that generally last less than or equal to 7 days (most less than 24 h); 2, usually more than 7 days; 3, cardioversion failed or not attempted; and 4, either paroxysmal or persistent AF may be recurrent.

concurrently with management of the episode of AF usually eliminates the arrhythmia.

IV. Epidemiology and Prognosis

AF is the most common clinically significant cardiac arrhythmia. In one series, AF accounted for 34.5% of patients hospitalized with a cardiac rhythm disturbance (5). It has been estimated that 2.2 million Americans have paroxysmal or persistent AF (6).

A. Prevalence

The prevalence of AF is estimated at 0.4% of the general population, increasing with age (7). AF is uncommon in childhood except after cardiac surgery. It occurs in fewer than 1% of those under 60 years of age but in more than 6% of those over 80 years of age (8–10) (Fig. 2). The age-adjusted prevalence is higher in men (10,11). Blacks have less than half the age-adjusted risk of developing AF that is seen in whites (12). The frequency of lone AF was less than 12% of all cases of AF in some series (4,10,13,14) but over 30% in others (15,16). The prevalence of AF increases with the severity of congestive heart failure (HF) or valvular heart disease.

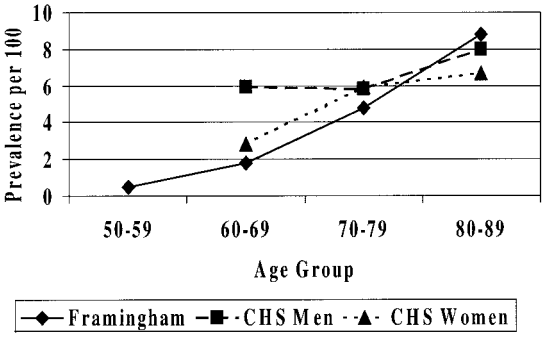

Figure 2. Prevalence of AF in 2 American epidemiological studies. Framingham indicates the Framingham Heart Study (9); CHS, Cardiovascular Health Study (10).

B. Prognosis

The rate of ischemic stroke among patients with nonrheumatic AF averages 5% per year, which is 2 to 7 times the rate for people without AF (8,9,15,17–19) (Fig. 3). One of every 6 strokes occurs in patients with AF (20). Including transient ischemic attacks and clinically silent strokes detected radiographically, the rate of brain ischemia accompanying nonvalvular AF exceeds 7% per year (21–25). In the Framingham Heart Study, patients with rheumatic heart disease and AF had a 17-fold increased risk of stroke compared with age-matched controls (26), and the attributable risk was 5 times greater than in those with nonrheumatic AF (9). Among AF patients from general practices in France, the ALFA Study (Etude en Activité Liberale sur le Fibrillation Auriculaire) found a 2.4% incidence of thromboembolism over a mean of 8.6 months of follow-up (15). The annual risk of stroke attributable to AF increased from 1.5% in Framingham Study participants aged 50 to 59 years to 23.5% for those aged 80 to 89 years (9). The total mortality rate is approximately doubled in patients with AF compared with patients in normal sinus rhythm and is linked with the severity of underlying heart disease (8,11,18) (Fig. 3).

V. Pathophysiological Mechanisms

A. Atrial Factors

1. Pathology of the Atrium in Patients With AF

The atria of patients with persistent AF display structural abnormalities beyond those caused by underlying heart disease (27). Patchy fibrosis with juxtaposition of normal and diseased atrial fibers may account for nonhomogeneity of atrial refractoriness (28,29). Fibrosis or fatty infiltration can also affect the sinus node and might be a reaction to inflammatory or degenerative processes that are difficult to detect. The role of inflammation in the pathogenesis of AF has not yet been evaluated, but histological changes consistent with myocarditis were reported in 66% of biopsy specimens from patients with lone AF (29). Infiltration of the atrial

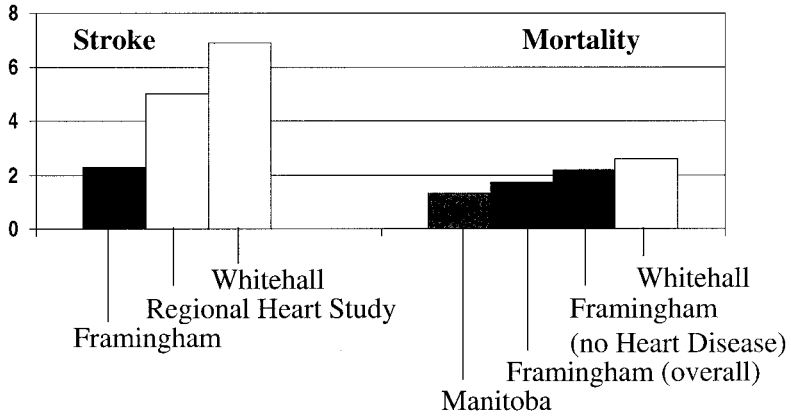

Figure 3. Relative risk of stroke and mortality in patients with AF compared with patients without AF. Source data are from the Framingham Heart Study (11), Regional Heart Study (8), Whitehall study (8), and Manitoba study (18).

myocardium can occur in amyloidosis, sarcoidosis, and hemochromatosis. Atrial fiber hypertrophy has been described as a major and sometimes the sole histological feature (28). Progressive atrial dilatation has been demonstrated echocardiographically in patients with AF (30) and, like hypertrophy, can be either a cause or a consequence of persistent AF.

2. Mechanisms of AF

Theories of the mechanism of AF involve 2 main processes: enhanced automaticity in 1 or several rapidly depolarizing foci and reentry involving 1 or more circuits (31,32). Rapidly firing atrial foci, located in 1 or several of the superior pulmonary veins, can initiate AF in susceptible patients (3,33). Foci also occur in the RA and infrequently in the superior vena cava or coronary sinus (3,33,34). The focal origin appears to be more important in paroxysmal AF than in persistent AF. Ablation of such foci can be curative (3).

The multiple-wavelet hypothesis as the mechanism of reentrant AF was advanced by Moe and colleagues (31,35), who proposed that fractionation of the wave fronts as they propagate through the atria results in self-perpetuating "daughter wavelets." The number of wavelets present at any time depends on the refractory period, mass, and conduction velocity in different parts of the atria.

Although the patterns of activation underlying the irregular atrial electrical activity of AF have traditionally been described as disorganized or random, recent evidence has emerged that AF is spatially organized. Based on mapping studies of patients undergoing surgery for the Wolff-Parkinson-White (WPW) syndrome, 3 patterns of induced AF have been identified (36). Type I AF involves single wave fronts propagating across the RA. Type II AF involves 1 or 2 wave fronts, and type III AF is characterized by multiple activation wavelets propagating in different directions. Ultimately, a better understanding of electrophysiological mechanisms will lead to the development of effective preventive measures (37).

B. AV Conduction

1. General Aspects

The AV node is ordinarily the factor that limits conduction during AF. The compact AV node is located anteriorly in the triangle of Koch (38), surrounded by transitional cells. There appear to be 2 distinct atrial inputs to the AV node, posteriorly via the crista terminalis and anteriorly via the interatrial septum. Studies on rabbit AV nodal preparations show that during AF, propagation of impulses through the AV node to the His bundle depends in part on the relative timing of the anterior and posterior septal activation inputs to the AV node (39). Other factors that affect conduction through the AV node are its intrinsic conduction and refractoriness, concealed conduction, and autonomic tone.

2. AV Conduction in the WPW Syndrome

Accessory pathways are muscle connections between the atrium and ventricle that have the capacity to conduct rapidly. Conduction over an accessory pathway during AF can result in a very rapid ventricular response that can be fatal (2,40).

Drugs such as digitalis, calcium channel antagonists, and beta-blockers, which are usually given to slow conduction across the AV node during AF, do not block conduction over the accessory pathway and can even enhance conduction, resulting in hypotension or cardiac arrest (41). Patients who develop AF with a rapid ventricular response associated with hemodynamic instability that results from conduction over an accessory pathway should undergo immediate electrical cardioversion. In the absence of hemodynamic instability or a preexcited ventricular response, intravenous procainamide and ibutilide are drugs of choice to achieve pharmacological cardioversion or to block conduction over the accessory pathway.

C. Myocardial and Hemodynamic Consequences of AF

During AF, 3 factors can affect hemodynamic function: loss of synchronous atrial mechanical activity, irregularity of ventricular response, and inappropriately rapid heart rate. A marked decrease in cardiac output can occur with the loss of atrial contraction, especially in patients with impaired diastolic ventricular filling, hypertension, mitral stenosis, hypertrophic cardiomyopathy (HCM), or restrictive cardiomyopathies. The variation in RR intervals during AF can also result in hemodynamic impairment. A persistently rapid atrial rate can adversely affect atrial mechanical function (tachycardia-

induced atrial cardiomyopathy) (2,42). Such changes in atrial tissue might explain the delayed recovery of atrial contractility in patients after cardioversion to sinus rhythm.

A persistently elevated ventricular rate during AF (130 bpm or faster in one study) (43) can produce dilated ventricular cardiomyopathy (2,43–46). It is critically important to recognize tachycardia-induced cardiomyopathy, because control of the ventricular rate can lead to partial or even complete reversal of the myopathic process. In fact, HF can be the initial manifestation of AF. A variety of hypotheses have been proposed to explain tachycardia-mediated cardiomyopathy that involve myocardial energy depletion, ischemia, abnormalities of calcium regulation, and remodeling, but the actual mechanisms responsible for this disorder are still unclear (47).

D. Thromboembolism

Although ischemic stroke and systemic arterial occlusion in AF are generally attributed to embolism from the left atrium (LA), the pathogenesis of thromboembolism is complex (48). Up to 25% of AF-associated strokes can be due to intrinsic cerebrovascular diseases, other cardiac sources of embolism, or atheromatous pathology in the proximal aorta (49,50). About half of elderly AF patients have chronic hypertension (a major risk factor for cerebrovascular disease) (19), and approximately 12% harbor cervical carotid artery stenosis. Carotid atherosclerosis is not substantially more prevalent in AF patients with stroke than in patients without AF, however, and is probably a relatively minor contributing factor (51).

1. Pathophysiology of Thrombus Formation

Thrombus associated with AF arises most frequently in the LA appendage (LAA). This cannot be examined reliably by precordial (transthoracic) echocardiography (52), whereas transesophageal Doppler echocardiography provides a sensitive and specific method to assess LAA function (53) and to detect thrombotic material. LAA flow velocities are reduced because of loss of organized mechanical contraction during AF (54,55). This substrate of decreased flow within the LA/LAA has been associated with spontaneous echo contrast, thrombus formation, and embolic events (56–62). LAA flow velocities are lower in patients with atrial flutter than what is usually seen with normal sinus rhythm but are higher than with AF. Whether this accounts for the slightly lower prevalence of LAA thrombus and perhaps a lower rate of thromboembolism associated with atrial flutter is uncertain.

In patients with AF, independent predictors of spontaneous echo contrast include LA size, LAA flow velocity (56,63), left ventricular (LV) dysfunction, fibrinogen level (62), hematocrit (61,62), and aortic atherosclerosis (61,62,64,65). This phenomenon might be an echocardiographic surrogate for regional coagulopathy and, when dense, is of clinical value to identify AF patients at high risk for thromboembolism (64), but its utility for prospective risk stratification for thromboembolism beyond that achieved by clinical assessment has not been established. Although conventional clinical management is based on the presumption that thrombus formation requires continuation of AF for approximately 48 h, thrombi have been identified by transesophageal echocardiography (TEE) within shorter intervals (66,67).

Contrary to the prevalent view that systemic anticoagulation for 4 weeks results in endocardial adherence and organization of LAA thrombus, TEE studies have verified resolution of thrombus in the majority of patients (68). Similar observations have defined the transient nature of LA/LAA dysfunction on conversion of AF, which provides a mechanistic rationale for anticoagulation for several weeks before and after successful cardioversion.

2. Clinical Implications

Because the pathophysiology of thromboembolism in patients with AF is uncertain, the mechanisms that link risk factors to ischemic stroke in AF are also incompletely defined. The strong association between hypertension and stroke in AF is probably mediated primarily by embolism that originates in the LAA (49), but hypertension also increases the risk of noncardioembolic strokes in AF (49,69). Hypertension in AF patients is associated with reduced LAA flow velocity and spontaneous echo contrast, which predisposes the patient to thrombus formation (63,64,70). Ventricular diastolic dysfunction might underlie the effect of hypertension on LA dynamics (71,72). The effect of advancing age to increase stroke risk in AF is multifactorial. In patients with AF, aging is associated with LA enlargement, reduced LAA flow velocity, and spontaneous echo contrast, each of which predisposes to LA thrombus formation (30,63,64). Additionally, age is a risk factor for atherosclerosis, including complex aortic arch plaque, and is associated with stroke independently of AF (65). LV systolic dysfunction predicts ischemic stroke in AF patients receiving no antithrombotic therapy (73–76).

VI. Associated Conditions, Clinical Manifestations, and Quality of Life

A. Causes and Associated Conditions

1. Acute Causes of AF

AF can be related to acute, temporary causes, including alcohol intake, surgery, electrocution, myocarditis, pulmonary embolism, other pulmonary diseases, and hyperthyroidism. Successful treatment of the underlying condition can eliminate AF. AF is a common early postoperative complication of myocardial infarction and of cardiac or thoracic surgery.

2. AF Without Associated Cardiovascular Disease

In younger patients, approximately 30% to 45% of paroxysmal cases and 20% to 25% of persistent cases of AF occur as lone AF (13,15,16).

3. AF With Associated Cardiovascular Disease

Specific cardiovascular conditions associated with AF include valvular heart disease (most often mitral), coronary artery disease (CAD), and hypertension, particularly when LV hypertrophy (LVH) is present.

4. Neurogenic AF

The autonomic nervous system can trigger AF in susceptible patients through heightened vagal or adrenergic tone.

Many patients experience onset of AF during periods of enhanced parasympathetic or sympathetic tone. Coumel (77) described a group of patients that he characterized in terms of a vagal or adrenergic form of AF. Patients with pure vagal or adrenergic AF are uncommon, but if the history reveals a pattern of onset of AF with features of one of these syndromes, the clinician can select agents more likely to prevent recurrent episodes.

B. Clinical Manifestations

AF can be symptomatic or asymptomatic, even in the same patient. Symptoms vary with the ventricular rate, underlying functional status, duration of AF, and individual patient perceptions. The dysrhythmia can present for the first time with an embolic complication or exacerbation of HF. Most patients with AF complain of palpitations, chest pain, dyspnea, fatigue, or lightheadedness. Release of atrial natriuretic peptide can be associated with polyuria. AF can lead to tachycardia-mediated cardiomyopathy, especially in patients who are unaware of the arrhythmia. Syncope is an uncommon but serious complication that usually indicates sinus node dysfunction, valvular aortic stenosis, HCM, cerebrovascular disease, or an accessory AV pathway.

C. Quality of Life

Although strokes certainly account for much of the functional impairment associated with AF, the rhythm disturbance also decreases quality of life. In the Stroke Prevention in Atrial Fibrillation (SPAF) study cohort, the New York Heart Association functional classification, developed for HF, was an insensitive index of quality of life in patients with AF (78). In another study (79), 47 (68%) of 69 patients with paroxysmal AF considered the dysrhythmia disruptive of their lives. This perception was not associated with either the frequency or duration of symptoms. The AFFIRM trial (Atrial Fibrillation Follow-up Investigation of Rhythm Management), which is still in progress, is comparing maintenance of sinus rhythm with rate control in patients with AF, addressing many facets of quality of life, as did the smaller PIAF (Pharmacological Intervention in Atrial Fibrillation) study (80). In selected patients, radiofrequency catheter ablation of the AV node and pacemaker insertion improved quality-of-life scores compared with medical therapy (81–86).

Long-term oral anticoagulant therapy, which involves frequent blood testing and multiple drug interactions, is another factor with important implications for the quality of life of AF patients. Decision analysis found that only 61% of 97 patients preferred anticoagulation therapy to no treatment (87), a considerably smaller proportion than that for whom treatment has been recommended according to published guidelines.

VII. Clinical Evaluation

A. Minimum Evaluation of the Patient With AF

1. Clinical History and Physical Examination

The initial evaluation of a patient with suspected or proven AF includes characterizing the pattern of the arrhythmia as paroxysmal or persistent, determining its cause, and defining associated cardiac and extracardiac factors (Table 1). A careful history will result in a well-planned, focused workup that serves as an effective guide to therapy (2). The workup of an AF patient can usually take place and therapy can be initiated in 1 outpatient encounter. Delay occurs when the rhythm has not been specifically documented and additional monitoring is necessary.

The physical examination may suggest AF on the basis of irregular pulse, irregular jugular venous pulsations, and variation in the loudness of the first heart sound. Examination may also disclose associated valvular heart disease, myocardial abnormalities, or HF. The findings on examination are similar in patients with atrial flutter, except that the rhythm may be regular and rapid venous oscillations may occasionally be visible in the jugular pulse.

2. Investigations

The diagnosis of AF requires ECG documentation by at least single-lead ECG recording during the dysrhythmia, which may be facilitated by review of emergency department records, Holter monitoring, or transtelephonic or telemetric recordings. A portable ECG recording tool may help establish the diagnosis in cases of paroxysmal AF and provide a permanent ECG record of the dysrhythmia. If episodes are frequent, then a 24-h Holter monitor can be used. If episodes are infrequent, then an event recorder, which allows the patient to transmit the ECG to a recording facility when the arrhythmia occurs, may be more useful.

B. Additional Investigation of Selected Patients With AF

Additional investigation may include Holter monitoring and exercise testing, transesophageal echocardiography, and/or electrophysiological study. See Table 1 for details.

VIII. Management

The major issues in management of patients with AF are related to the arrhythmia itself and to prevention of thromboembolism. In patients with persistent AF, there are fundamentally 2 ways to manage the dysrhythmia: to restore and maintain sinus rhythm or to allow AF to continue and ensure that the ventricular rate is controlled.

A. Rhythm Control vs Heart Rate Control

Reasons for restoration and maintenance of sinus rhythm in patients with AF include relief of symptoms, prevention of embolism, and avoidance of cardiomyopathy.

B. Cardioversion

1. Basis for Cardioversion of AF

Cardioversion is often performed electively to restore sinus rhythm in patients with persistent AF. The need for cardioversion can be immediate, however, when the arrhythmia is the main factor responsible for acute HF, hypotension, or worsening of angina pectoris in a patient with CAD. Nevertheless, cardioversion carries a risk of thromboembolism unless anticoagulation prophylaxis is initiated before the procedure, and this risk appears to be greatest when the arrhythmia has been present more than 48 h.

TABLE 1. Minimum and Additional Clinical Evaluation of Patients With Atrial Fibrillation

Minimum evaluation

1. History and physical examination, to define
   - The presence and nature of symptoms associated with AF
   - The clinical type of AF (first episode, paroxysmal, persistent, or permanent)
   - The onset of the first symptomatic attack or date of discovery of AF
   - The frequency, duration, precipitating factors, and modes of termination of AF
   - The response to any pharmacological agents that have been administered
   - The presence of any underlying heart disease or other reversible conditions (eg, hyperthyroidism or alcohol consumption)
2. Electrocardiogram, to identify
   - Rhythm (verify AF)
   - LV hypertrophy
   - P-wave duration and morphology or fibrillatory waves
   - Preexcitation
   - Bundle-branch block
   - Prior MI
   - Other atrial arrhythmias
   - To measure and follow the RR, QRS, and QT intervals in conjunction with antiarrhythmic drug therapy
3. Chest radiograph, to evaluate
   - The lung parenchyma, when clinical findings suggest an abnormality
   - The pulmonary vasculature, when clinical findings suggest an abnormality
4. Echocardiogram, to identify
   - Valvular heart disease
   - Left and right atrial size
   - LV size and function
   - Peak RV pressure (pulmonary hypertension)
   - LV hypertrophy
   - LA thrombus (low sensitivity)
   - Pericardial disease
5. Blood tests of thyroid function
   - For a first episode of AF, when the ventricular rate is difficult to control, or when AF recurs unexpectedly after cardioversion

Additional testing

- One or several tests may be necessary

1. Exercise testing
   - If the adequacy of rate control is in question (permanent AF)
   - To reproduce exercise-induced AF
   - To exclude ischemia before treatment of selected patients with a type IC antiarrhythmic drug
2. Holter monitoring or event recording
   - If diagnosis of the type of arrhythmia is in question
   - As a means of evaluating rate control
3. Transesophageal echocardiography
   - To identify LA thrombus (in the LA appendage)
   - To guide cardioversion
4. Electrophysiological study
   - To clarify the mechanism of wide-QRS-complex tachycardia
   - To identify a predisposing arrhythmia such as atrial flutter or paroxysmal supraventricular tachycardia
   - Seeking sites for curative ablation or AV conduction block/modification

AF indicates atrial fibrillation; LV, left ventricular; MI, myocardial infarction; RV, right ventricular; LA, left atrial; and AV, atrioventricular. Type IC refers to the Vaughan Williams classification of antiarrhythmic drugs (see Table 2).

2. Methods of Cardioversion

Cardioversion can be achieved by means of drugs or electrical shocks. Drugs were commonly used before electrical cardioversion became a standard procedure. The development of new drugs has increased the popularity of pharmacological cardioversion, although some disadvantages persist, including the risk of drug-induced torsade de pointes ventricular tachycardia or other serious arrhythmias. Pharmacological cardioversion is still less effective than electrical cardioversion, but the latter requires conscious sedation or anesthesia, whereas the former does not.

The risk of thromboembolism or stroke does not differ between pharmacological and electrical cardioversion. Thus, recommendations for anticoagulation are the same for both methods.

C. Pharmacological Cardioversion

Pharmacological cardioversion appears to be most effective when initiated within 7 days after the onset of AF (88–91). Most such patients have paroxysmal AF, a first-documented episode of AF, or an unknown pattern of AF at the time of treatment. (See Section III, Classification.) A large proportion of patients with recent-onset AF experience spontaneous cardioversion within 24 to 48 h (92–94). This is less likely to occur when AF has persisted for more than 7 days.

The relative efficacy of various drugs differs for pharmacological cardioversion of AF and atrial flutter, yet many studies of drug therapy for AF have included patients with atrial flutter. The dose, route, and rapidity of administration influence efficacy. Reference is made to the Vaughan Williams classification of antiarrhythmic drugs (95), which has been modified to include recently available drugs (Table 2). A summary of recommendations is presented in Tables 10 through 12 (see Section IX-B, Recommendations for Pharmacological and Electrical Cardioversion of AF, Tables 10–12). Although clinical use of the antiarrhythmic drugs listed has been approved by regulatory agencies, therapeutic use for AF has not been mentioned or approved in all cases in each country. The recommendations given in this document do not necessarily adhere to governmental regulations and labeling requirements.

A frequent issue related to pharmacological cardioversion is whether the antiarrhythmic drug should be started in the hospital or on an outpatient basis. The major concern is the potential for serious adverse effects, including torsade de pointes ventricular tachycardia. With the exception of those involving low-dose oral amiodarone (96), virtually all studies of pharmacological cardioversion have been limited to hospitalized patients.

D. Electrical Cardioversion

Direct-current cardioversion involves an electrical shock synchronized with the intrinsic activity of the heart. This ensures that electrical stimulation does not occur during the vulnerable phase of the cardiac cycle (97).

Successful cardioversion of AF depends on the nature of the underlying heart disease and the current density delivered to the atrial myocardium. The latter, in turn, depends on the voltage of the defibrillator capacitor, the output waveform, the size and position of the electrode paddles, and transthoracic impedance.

TABLE 2. Vaughan Williams Classification of Antiarrhythmic Drug Actions

Type IA
Disopyramide
Procainamide
Quinidine
Type IB
Lidocaine
Mexiletine
Type IC
Flecainide
Moricizine
Propafenone
Type II
Beta-blockers (e.g., propranolol)
Type III
Amiodarone
Bretylium
Dofetilide
Ibutilide
Sotalol
Type IV
Calcium-channel antagonists (e.g., verapamil and diltiazem)

Modified with permission from Vaughn Williams EM. A classification of antiarrhythmic action as reassessed after a decade of new drugs. J Clin Pharmacol 1984;24:129–47, © 1984 by Sage Publications Inc. (95) to include compounds introduced after publication of the original classification.

In a randomized controlled study of 301 subjects undergoing elective external cardioversion, patients were allocated to anterior-lateral (ventricular apex and right infraclavicular) or anterior-posterior (sternum and left scapular) paddle positions (98). The energy requirement was lower and overall success was greater with the anterior-posterior configuration (87%) than with the anterior-lateral alignment (76%).

Cardioversion is performed with the patient having fasted and under adequate anesthesia. Short-acting anesthetic agents are preferred, because cardioversion patients are well suited to day care and should recover rapidly after the procedure (99).

An initial shock of 100 J is often too low, and an initial energy of 200 J or greater is recommended for electrical cardioversion of AF. Devices that deliver current with a biphasic waveform appear to achieve cardioversion at lower energy levels than those that use a monophasic waveform. The primary success rate as measured 3 days after cardioversion in 100 consecutive subjects was 86% (100); this increased to 94% when the procedure was repeated during treatment with quinidine or disopyramide. Only 23% of the patients remained in sinus rhythm after 1 year and 16% after 2 years; in those who relapsed, repeated cardioversion with antiarrhythmic medication resulted in sinus rhythm in 40% and 33% after 1 and 2 years, respectively. For patients who relapsed again, a third cardioversion resulted in sinus rhythm

in 54% at 1 year and 41% at 2 years. Thus, sinus rhythm can be restored in a substantial proportion of patients by direct-current cardioversion, but the rate of relapse is high unless antiarrhythmic drug therapy is given concomitantly.

Cardioversion of patients with implanted pacemaker and defibrillator devices is safe when appropriate precautions are taken. The device should be interrogated immediately before and after cardioversion to verify appropriate function. The paddles used for external cardioversion should be positioned as distant as possible from the device, preferably in the anterior-posterior configuration.

The risks of electrical cardioversion are mainly related to embolic events and cardiac arrhythmias. Thromboembolic events have been reported in 1% to 7% of patients who did not receive anticoagulation before cardioversion (101,102). Various brief arrhythmias might arise, especially ventricular and supraventricular premature beats, bradycardia, and short periods of sinus arrest (103). Ventricular tachycardia and fibrillation can be precipitated in patients with hypokalemia or digitalis intoxication (104,105). A slow ventricular response to AF in the absence of drugs that slow AV nodal conduction can indicate conduction defect. The patient should be evaluated before cardioversion with these issues in mind to avoid symptomatic bradycardia (106). Transient ST-segment elevation can appear on the ECG after cardioversion (107–108) and blood levels of creatine kinase-MB can rise even without apparent myocardial damage.

Prophylactic drug therapy to prevent early recurrence of AF should be considered individually for each patient. Should relapse (particularly early relapse) occur, antiarrhythmic therapy is recommended in conjunction with the second attempt. Further cardioversion is of limited value. In highly symptomatic patients, infrequently repeated cardioversion can be an acceptable approach.

E. Maintenance of Sinus Rhythm

1. Pharmacological Therapy to Prevent Recurrence of AF

Maintenance of sinus rhythm is relevant in patients with paroxysmal AF (in whom episodes terminate spontaneously) and persistent AF (in whom electrical or pharmacological cardioversion is necessary to restore sinus rhythm). Whether paroxysmal or persistent, AF is a chronic disorder, and recurrence is likely at some point in most patients (Fig. 4) (109,110). Prophylactic treatment with antiarrhythmic drugs is therefore often necessary. The goal of maintenance therapy is suppression of symptoms and sometimes prevention of tachycardia-induced cardiomyopathy due to AF. It is not yet known whether maintenance of sinus rhythm prevents thromboembolism, HF, or death (80,111).

Recurrence of AF is not equivalent to treatment failure. In several studies (112,113), patients with recurrent AF often chose to continue drug treatment. Sometimes, reduction of the arrhythmia burden can constitute partial success, whereas to other patients, any recurrence of AF may seem intolerable. Nevertheless, most patients with AF eventually experience recurrence. Risk factors for frequent recurrence of paroxysmal AF (more than 1 episode per month) include female sex and underlying heart disease (114). In persistent AF, the

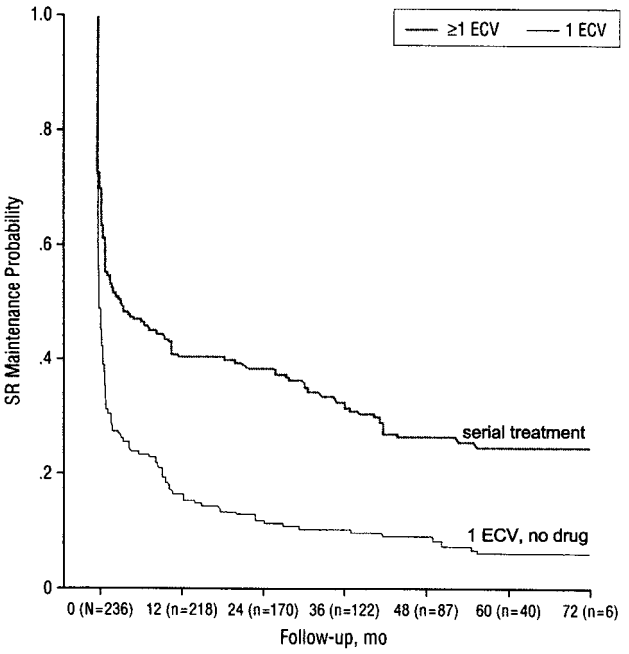

Figure 4. Arrhythmia-free survival after electrical cardioversion in patients with persistent atrial fibrillation. The lower curve represents outcome after a single shock when no prophylactic drug therapy was given. The upper curve depicts the outcome with repeated electrical cardioversions in conjunction with antiarrhythmic drug prophylaxis. ECV indicates electrical cardioversion; SR, sinus rhythm. Reproduced with permission from van Gelder et al., Arch Intern Med 1996;156:2585–92, © 1996, American Medical Association (110).

4-year arrhythmia-free survival was less than 10% after single-shock electrical cardioversion without prophylactic drug therapy (110). Predictors of recurrences within that interval included hypertension, age greater than 55 years, and AF duration greater than 3 months. In that study, serial cardioversions and prophylactic drug therapy resulted in freedom from recurrent AF in only approximately 30% of patients (110). Predictors of recurrence included age greater than 70 years, AF duration greater than 3 months, and HF (110).

2. General Approach to Antiarrhythmic Drug Therapy

Before any antiarrhythmic agent is administered, reversible cardiovascular and noncardiovascular precipitants of AF should be addressed. Prophylactic drug treatment is seldom indicated in case of a first-detected episode of AF and can also be avoided in patients with infrequent and well-tolerated paroxysmal AF. Similarly, when recurrences are infrequent and tolerated, patients experiencing breakthrough arrhythmias might not require a change in antiarrhythmic drug therapy. Beta-blockers can be effective in patients who develop AF only during exercise, but few patients have a single specific inciting cause for all episodes of AF, and a majority will not sustain sinus rhythm without antiarrhythmic drug treatment.

In patients with lone AF, a beta-blocker may be tried first, but flecainide, propafenone, and sotalol are particularly effective. Amiodarone and dofetilide are recommended as alternative therapy. Quinidine, procainamide, and disopyr-

TABLE 3. Typical Doses of Drugs Used to Maintain Sinus Rhythm in Patients With Atrial Fibrillation**

Drug*	Daily Dosage	Potential Adverse Effects
Amiodarone†	100–400 mg	Photosensitivity, pulmonary toxicity, polyneuropathy, GI upset, bradycardia, torsade de pointes (rare), hepatic toxicity, thyroid dysfunction
Disopyramide	400–750 mg	Torsade de pointes, HF, glaucoma, urinary retention, dry mouth
Dofetilide‡	500–1000 mcg	Torsade de pointes
Flecainide	200–300 mg	Ventricular tachycardia, congestive HF, enhanced AV nodal conduction (conversion to atrial flutter)
Procainamide	1000–4000 mg	Torsade de pointes, lupus-like syndrome, GI symptoms
Propafenone	450–900 mg	Ventricular tachycardia, congestive HF, enhanced AV nodal conduction (conversion to atrial flutter)
Quinidine	600–1500 mg	Torsade de pointes, GI upset, enhanced AV nodal conduction
Sotalol‡	240–320 mg	Torsade de pointes, congestive HF, bradycardia, exacerbation of chronic obstructive or bronchospastic lung disease

GI indicates gastrointestinal; AV, atrioventricular; and HF, heart failure.
*Drugs are listed alphabetically.
**The drugs and doses given here have been determined by consensus based on published studies.
†A loading dose of 600 mg per day is usually given for one month or 1000 mg per day over 1 week.
‡Dose should be adjusted for renal function and QT-interval response during in-hospital initiation phase.

amide are not favored unless amiodarone fails or is contraindicated. The anticholinergic activity of long-acting disopyramide makes this a relatively attractive choice for patients with a predilection to vagally induced AF. Propafenone is not recommended in vagally mediated AF because its (weak) intrinsic beta-blocking activity might aggravate this type of paroxysmal AF. In patients with adrenergically mediated AF, beta-blockers represent first-line treatment, followed by sotalol and amiodarone. In patients with adrenergically mediated lone AF, amiodarone should be chosen later in the sequence of drug therapy because of its potential toxicity (see Fig. 11, Section IX). Overall, when treatment with a single drug fails, combinations of antiarrhythmic drugs may be tried. Useful combinations include a beta-blocker, sotalol or amiodarone, plus a type IC agent.

A drug that is initially safe might become proarrhythmic when the patient develops CAD or HF or begins taking other medication that in combination can be arrhythmogenic. Thus, the patient should be alerted to the potential significance of such symptoms as syncope, angina pectoris, or dyspnea and warned about the use of noncardiac drugs that can prolong the QT interval. A useful source of information is the Internet site http://www.torsades.org.

Monitoring of antiarrhythmic drug treatment varies with the agent involved and with patient factors. Prospective trial data on upper limits of drug-induced increases in QRS duration or QT prolongation are not available. The following recommendations are the consensus of the writing committee. With type IC drugs, QRS widening should not exceed 150% of the pretreatment QRS duration. Exercise testing can be helpful to detect QRS widening that occurs only at rapid heart rates (use-dependent conduction slowing). For type IA or type III drugs, with the possible exception of amiodarone, the corrected QT interval in sinus rhythm should remain below 520 ms. During follow-up, plasma potassium and magnesium levels and renal function should be checked periodically, because renal insufficiency leads to drug accumulation and predisposes to proarrhythmia. In individual patients, serial noninvasive tests can be appropriate to reevaluate LV function, especially if clinical HF develops during treatment of AF.

3. Pharmacological Agents to Maintain Sinus Rhythm

Fourteen controlled trials of drug prophylaxis involving patients with paroxysmal AF have been published, and there have been 22 published trials of drug prophylaxis for maintenance of sinus rhythm in patients with persistent AF. Comparative data are not sufficient to permit subclassification by drug or etiology. Individual drugs and dosages for maintenance of sinus rhythm are given in Table 3.

4. Out-of-Hospital Initiation of Antiarrhythmic Drugs in Patients With AF

Recommendations for out-of-hospital initiation or intermittent use of antiarrhythmic drugs differ for patients with paroxysmal and persistent AF. In patients with paroxysmal AF, the aims are to stop an attack, to prevent recurrences, or a combination of both. In patients with persistent AF, the aims of out-of-hospital drug initiation are to achieve pharmacological cardioversion of AF, thereby obviating the need for electrical cardioversion, or to enhance the success of electrical cardioversion and prevent early recurrence of AF.

Few prospective data are available on the safety of outpatient initiation of antiarrhythmic drug therapy. Proarrhythmia (Table 4) is rare in patients with normal ventricular function and baseline QT intervals (41,115) without profound bradycardia. As long as sinus or AV node dysfunction is not suspected, propafenone or flecainide may be initiated out of hospital. Sudden death related to idiopathic ventricular fibril-

TABLE 4. Types of Proarrhythmia During Treatment With Various Antiarrhythmic Drugs for Atrial Fibrillation or Atrial Flutter According to the Vaughan Williams Classification

A. Ventricular proarrhythmia
• Torsade de pointes (VW type IA and type III drugs)
• Sustained monomorphic ventricular tachycardia (usually VW type IC drugs)
• Sustained polymorphic ventricular tachycardia/VF without long QT (VW types IA, IC, and III drugs)
B. Atrial proarrhythmia
• Provocation of recurrence (probably VW types IA, IC, and III drugs)
• Conversion of AF to flutter usually VW type IC drugs)
• Increase of defibrillation threshold (a potential problem with VW type IC drugs)
C. Abnormalities of conduction or impulse formation
• Acceleration of ventricular rate during AF (VW type IA and type IC drugs)
• Accelerate conduction over accessory pathway (digoxin, intravenous verapamil or diltiazem)
• Sinus node dysfunction and atrioventricular block (almost all drugs)

VW indicates the Vaughan Williams classification of antiarrhythmic drugs (95). VF indicates ventricular fibrillation; AF, atrial fibrillation.

lation in a structurally normal heart can occur in patients with the Brugada syndrome, an inherited cardiac disease characterized by ST-segment elevation in the right precordial ECG leads and frequently accompanied by right bundle-branch block. Type I antiarrhythmic drugs can unmask this condition (116,117). Before therapy with these agents is begun, a beta-blocker or calcium channel antagonist should be given to prevent rapid AV conduction or 1:1 AV conduction if atrial flutter develops (118–122). Because termination of paroxysmal AF with flecainide or propafenone can be associated with bradycardia due to sinus node or AV node dysfunction, an initial conversion should be undertaken in the hospital before a patient is declared fit for outpatient "pill-in-the pocket" use of these agents for conversion of recurrences. Out-of-hospital drug termination should be avoided in patients with symptomatic sick sinus syndrome, AV conduction disturbances, or bundle-branch block.

Sotalol may be initiated in outpatients with little or no heart disease as long as the baseline uncorrected QT interval is less than 450 ms, serum electrolytes are normal, and none of the type III drug-related proarrhythmia risk factors are present. Safety is greatest when sotalol is started when the patient is in sinus rhythm. Amiodarone can usually be given safely on an outpatient basis, even in patients with persistent AF (123), but in-hospital loading might be more appropriate when earlier restoration of sinus rhythm is needed, as in patients with HF. Some loading regimens involve giving either 600 mg per day for 4 weeks (123) or greater than or equal to 1 g per day for 1 week (124) followed by lower maintenance doses. Quinidine, procainamide, and disopyramide should generally not be started out of hospital. An exception can be made for disopyramide in patients without heart disease who have a normal QT interval. Currently, the standards for use of dofetilide do not permit out-of-hospital initiation.

Transtelephonic monitoring or other ECG surveillance methods can be used to monitor conduction disturbances as

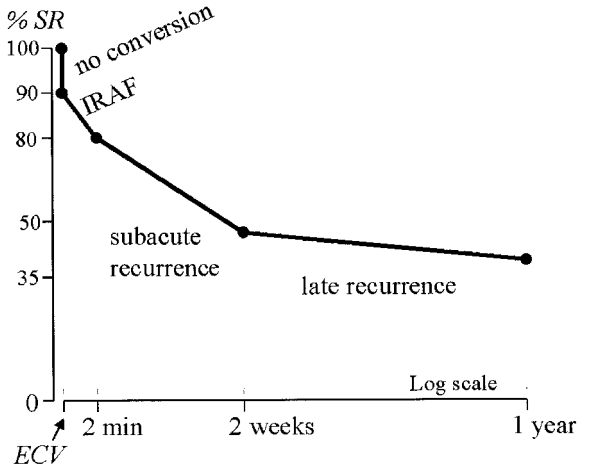

Figure 5. Hypothetical illustration of cardioversion failure.Three types of recurrences after electrical cardioversion of persistent AF are shown The efficacy of drugs varies in enhancement of shock conversion and suppression of recurrences ECV indicates external cardioversion; IRAF, first recurrence of AF after cardioversion. Modified with permission from Van Gelder et al (129).

pharmacological antiarrhythmic therapy is initiated in patients with AF. Specifically, the PR interval (flecainide, propafenone, sotalol, and amiodarone), QRS duration (flecainide and propafenone), and QT interval (sotalol, amiodarone, and disopyramide) should be measured. As a general rule, antiarrhythmic drugs should be started at a relatively low dose with upward titration as needed, reassessing the ECG as each dose change is made. The dose of other medication used for rate control should be reduced approximately 6 weeks after initiation of amiodarone and stopped if the rate slows excessively. Concomitant drug therapies should be monitored closely, and both the patient and the physician should be alert to possible deleterious drug interactions.

5. Recurrence of AF After Cardioversion: Implications for Drug Treatment

Although it has long been known that most recurrences of AF occur within the first month after electrical cardioversion, recent research with internal atrial cardioversion (125) and day-to-day postconversion studies (126) have established several patterns of recurrence (Fig. 5). In some cases, there is complete failure of direct-current countershock to elicit even a single isolated sinus or ectopic atrial beat, tantamount to a high atrial defibrillation threshold. In others, AF reappears within 1 to 2 minutes after a period of sinus rhythm (127,128). Sometimes recurrence is delayed from 1 day to 2 weeks (126) or more after the shock. Complete shock failure and immediate recurrences occur in approximately 25% of patients undergoing electrical cardioversion, and subacute recurrences occur in about an equal proportion within 2 weeks (127).

Available data suggest that starting pharmacological therapy before electrical cardioversion (Table 5) can enhance immediate success and suppress early recurrences. As a corollary, it seems appropriate to establish therapeutic plasma drug concentrations at the time of cardioversion and for a few weeks thereafter to optimize the chance of success. After cardioversion to sinus rhythm, patients receiving drugs that

TABLE 5. Pharmacological Treatment Before Cardioversion in Patients With Persistent Atrial Fibrillation: Effects of Various Antiarrhythmic Drugs on Acute and Subacute Outcome of Transthoracic Direct Current Shock

	Enhance Conversion by DC Shock and Prevent IRAF*	Suppress SRAF and Maintenance Therapy Class	Recommendation Class	Level of Evidence
Effective	Amiodarone Flecainide Ibutilide Propafenone Propafenone+verapamil Quinidine Sotalol	All drugs in recommendation Class I (except ibutilide) plus beta-blockers	I	B
Uncertain/unknown	Beta-blockers Disopyramide Diltiazem Dofetilide Procainamide Verapamil	Diltiazem Dofetilide Verapamil	IIb	B

All drugs (except beta-blockers and amiodarone) should be initiated in hospital. IRAF indicates immediate recurrence of atrial fibrillation; SRAF, subacute recurrence of atrial fibrillation; and DC, direct current.

*Drugs are listed alphabetically within each class of recommendation.

prolong QT interval should be observed in the hospital for 24 to 48 h to evaluate the effects of heart rate slowing and to allow prompt intervention in the event torsade de pointes develops. Pharmacological agents may be started out of hospital or in hospital immediately before electrical cardioversion. The risks of pretreatment include the possibility of a paradoxical increase in the defibrillation threshold, as has occurred with flecainide (130); accelerated ventricular rate during loading with type IA or IC drugs in the absence of an AV nodal blocking agent (118–122,131) and ventricular proarrhythmia (Table 4).

Pretreatment with pharmacological agents is most appropriate in patients who have previously failed to respond to electrical cardioversion and in those who developed immediate or subacute recurrence of AF. In patients with late recurrence and those undergoing initial cardioversion of persistent AF, pretreatment is optional (Fig. 10 and 11; see Section IX).

6. Selection of Antiarrhythmic Agents in Patients With Certain Cardiac Diseases

a. Heart Failure

Patients with congestive HF are particularly prone to the ventricular proarrhythmic effects of antiarrhythmic drugs. Randomized trials have demonstrated the safety of amiodarone and dofetilide (given separately) in patients with HF (132,133), and these are the recommended drugs for maintenance of sinus rhythm (Fig. 11; see Section IX).

b. Coronary Artery Disease

In stable patients with CAD, beta-blockers may be considered first, but their use is supported by only 2 studies (134–135); data on their efficacy for maintenance of sinus rhythm in patients with persistent AF after cardioversion are not convincing (134). Sotalol has substantial beta-blocking activity and can therefore be chosen as the initial antiarrhythmic agent in AF patients with ischemic heart disease, because it is associated with less long-term toxicity than amiodarone (Fig. 11; see Section IX). Both sotalol and amiodarone have reasonable short-term safety profiles, and amiodarone might be preferred in patients with HF (136–138). Flecainide (139) and propafenone are not recommended in these situations. Quinidine, procainamide, and disopyramide are considered third-line treatment choices in patients with CAD. Given the results of the DIAMOND-MI trial (Danish Investigations of Arrhythmias and Mortality on Dofetilide in Myocardial Infarction), dofetilide may be considered as a second-line rather than a third-line antiarrhythmic agent, but that study involved selected post-myocardial infarction patients in whom the antiarrhythmic benefit balanced the risk of proarrhythmic toxicity.

c. Hypertensive Heart Disease

Patients with LVH are at increased risk of developing torsade de pointes related to early ventricular afterdepolarizations (140–142). Thus, a drug that does not prolong the QT interval is preferable as first-line therapy, and in the absence of CAD or marked ventricular hypertrophy, propafenone and flecainide are reasonable choices (Fig. 11; Section IX). Amiodarone prolongs the QT interval but carries a very low risk of ventricular proarrhythmia; its extracardiac toxicity profile relegates it to second-line therapy in these individuals, but amiodarone becomes first-line therapy when marked LVH is present. When amiodarone and sotalol either fail or are inappropriate, disopyramide, quinidine, or procainamide can be used as alternatives.

d. WPW Syndrome

Radiofrequency ablation of the accessory pathway is the preferred therapy for patients with preexcitation syndromes and AF, but antiarrhythmic drugs might be useful. Digoxin should be avoided because of the risk of paradoxical acceleration of the ventricular rate during AF. Beta-blockers do not decrease conduction over accessory pathways during preexcited periods of AF.

7. Nonpharmacological Correction of AF

a. Surgical Ablation

Based on mapping studies of animal and human AF, Cox et al (143–146) developed a surgical procedure (maze operation) that controls AF in more than 90% of selected patients. The exact mechanism has not been established conclusively, but the creation of barriers to conduction within the RA and LA limits the amount of myocardium available to propagate reentrant wave fronts, thereby inhibiting sustained AF. Incisions encircling the pulmonary veins can prevent initiation of AF by isolating potentially arrhythmogenic foci near the pulmonary veins from the remainder of the atria or by isolating atrial regions with the shortest refractory periods. Modifications of the Cox maze operation involve encircling the pulmonary veins by surgical incisions within the LA and radial incisions in both atria that join the mitral and tricuspid valve annuli (147–149).

Surgical operations for AF have been successfully combined with operative correction of a variety of structural cardiac conditions. In patients with highly symptomatic AF who require open heart operations for valvular, ischemic, or congenital heart disease, consideration should be given to concomitant maze operation for AF or flutter, although this entails additional risk. The mortality rate of an isolated maze operation is less than 1%, but mortality is higher when the procedure is combined with other types of operative repair. The morbidity associated with the maze operation includes consequences common to median sternotomy and cardiopulmonary bypass, as well as a risk of short-term fluid retention (owing to reduced release of atrial natriuretic peptide), transient reduction in LA and RA transport function, and early postoperative atrial tachyarrhythmias. In addition, when the blood supply to the sinus node is disrupted, sinus node dysfunction might require permanent pacemaker implantation. Progressive iterations of these operations have reduced the risk of this complication to less than 10%.

b. Catheter Ablation

Based on the success of surgical approaches to AF, several catheter ablation strategies have been designed to produce similar effects (150–152). Ablation strategies limited to the RA produce marginal improvement (150), whereas linear ablation in the LA has been more successful. The recognition that foci triggering AF often originate within the pulmonary veins has led to ablation strategies that target this zone or electrically isolate the pulmonary vein from the LA. Other sites of arrhythmogenic foci have been found in the superior vena cava, the RA and LA, and the coronary sinus. Ablation of these foci eliminates or reduces the frequency of recurrent AF in more than 60% of patients, but the risk of recurrent AF after a focal ablation procedure is still 30% to 50% over the first year and even higher when more than 1 pulmonary vein is involved. Thus, many patients continue to require antiarrhythmic drug therapy after ablative therapy of AF (153). Potential complications of catheter ablation for AF include systemic embolism, pulmonary vein stenosis, pericardial effusion, cardiac tamponade, and phrenic nerve paralysis. Thus, although these procedures have produced promising results, they have not yet been widely applied.

Atrial flutter can develop not only as a distinct arrhythmia but also during antiarrhythmic drug therapy of AF, especially with type IC agents. Catheter ablation is more effective than antiarrhythmic drugs for treatment of atrial flutter, reducing the recurrence rate from 93% to 5% when used as first-line therapy (37). In addition, the risk of developing AF might also be lower after catheter ablation of atrial flutter than with pharmacological therapy (29% vs 60% over the first year).

c. Suppression of AF by Pacing

Although atrium-based pacing is associated with a lower risk of AF and stroke than ventricle-based pacing for patients requiring pacemakers for bradyarrhythmias, the use of pacing as a primary therapy for prevention of recurrent AF has not been validated.

d. Internal Atrial Cardioverter/Defibrillators

There has been an interest in internal cardioversion of AF for the past 10 years. Attempts have been made to find shock waveforms that reduce the energy requirements for cardioversion, making the shock tolerable to awake patients. One cardioverter (154) capable of atrial sensing and cardioversion as well as ventricular sensing and pacing was evaluated in 290 AF patients. The conversion rate to sinus rhythm was 93%. Another device, with dual-chamber sensing, pacing, and cardioversion/defibrillation capabilities and a maximum output of 27 J, is a ventricular defibrillator with atrial cardioversion capabilities. It was designed to treat both atrial and ventricular arrhythmias with pacing modalities before delivering low-energy shocks. Potential candidates for atrial cardioverter/defibrillators, mainly those with infrequent episodes of poorly tolerated AF, are often suitable for catheter ablation.

F. Rate Control During AF

1. Pharmacological Approach

An alternative to maintenance of sinus rhythm in patients with paroxysmal or persistent AF is control of the ventricular rate. In a recent randomized trial, the therapeutic strategies of rate versus rhythm control yielded similar clinical results with respect to symptoms in patients with AF, but exercise tolerance was better with rhythm control (111). The results of other studies comparing these 2 strategies are not yet available (80). The rate is generally considered controlled when the ventricular response is between 60 and 80 bpm at rest and between 90 to 115 bpm during moderate exercise (156,157). Heart rate variability during AF provides additional information about the status of the autonomic nervous system, which might have independent prognostic implications (158–161).

Negative chronotropic therapy of AF is based mainly on depression of conduction across the AV node. Sinus bradycardia and heart block occur in some patients with paroxysmal AF, particularly the elderly, as an unwanted effect of pharmacological intervention with beta-blockers, digitalis glycosides, or calcium channel antagonists. Table 6 outlines agents that may be administered to control the ventricular response to AF in an emergency setting. Table 7 outlines drugs that block AV nodal conduction; these drugs can be used to achieve rate control both at rest and during exercise or other types of cardiovascular stress. A combination of drugs

TABLE 6. Intravenous Pharmacological Agents for Heart Rate Control in Patients With Atrial Fibrillation

Drug*	Loading Dose	Onset	Maintenance Dose	Major Side Effects	Class Recommendation
Diltiazem	0.25 mg/kg IV over 2 min	2–7 min	5–15 mg per hour infusion	Hypotension, heart block, HF	I†
Esmolol‡	0.5 mg/kg over 1 min	5 min	0.05–0.2 $mgkg^{-1}min^{-1}$	Hypotension, heart block, bradycardia, asthma, HF	I
Metoprolol‡	2.5–5 mg IV bolus over 2 min; up to 3 doses	5 min	NA	Hypotension, heart block, bradycardia, asthma, HF	I†
Propranolol‡	0.15 mg/kg IV	5 min	NA	Hypotension, heart block, bradycardia, asthma, HF	I†
Verapamil	0.075–0.15 mg/kg IV over 2 min	3–5 min	NA	Hypotension, heart block, HF	I†
Digoxin	0.25 mg IV each 2 h, up to 1.5 mg	2 h	0.125–0.25 mg daily	Digitalis toxicity, heart block, bradycardia	IIb**

HF indicates heart failure.
*Drugs are listed alphabetically within each class of recommendation.
**Type I in congestive HF.
†Type IIb in congestive HF.
‡Only representative members of the type of beta-adrenergic antagonist drugs are included in the table, but other, similar agents could be used for this indication in appropriate doses.

is often necessary to achieve rate control in AF patients in the acute and chronic settings. Therapy often requires careful dose titration, and some patients develop symptomatic bradycardia that requires permanent pacing.

2. Nonpharmacological Regulation of AV Nodal Conduction and Pacing

Because ventricular pacing prolongs the AV nodal refractory period as a result of concealed retrograde penetration, it eliminates ventricular cycles longer than the pacing cycle length and reduces the number of short ventricular cycles related to rapid AV conduction during AF. As a result, ventricular pacing can be used as a strategy to reduce the irregularity of the ventricular rhythm (162). This modality can be useful for patients with marked variability in ventricular rates and for those who develop resting bradycardia during treatment with medications prescribed to control rapid ventricular rates with exertion. The precise role of pacemaker therapy to regulate the ventricular rate in patients with AF, however, remains controversial.

3. Nonpharmacological/AV Nodal Ablation

AV nodal ablation and permanent pacemaker implantation are highly effective means of improving symptoms in patients

TABLE 7. Recommendations for Use of Orally Administered Pharmacological Agents for Heart Rate Control in Patients With Atrial Fibrillation

Drug*	Loading Dose	Onset	Usual Maintenance Dose**	Major Side Effects	Recommendation
Digoxin	0.25 mg PO each 2 h; up to 1.5 mg	2 h	0.125–0.375 mg daily	Digitalis toxicity, heart block, bradycardia	I
Diltiazem	NA	2–4 h	120–360 mg daily in divided doses; slow release available	Hypotension, heart block, HF	I
Metoprolol†	NA	4–6 h	25–100 mg BID	Hypotension, heart block, bradycardia, asthma, HF	I
Propranolol†	NA	60–90 min	80–240 mg daily in divided doses	Hypotension, heart block, bradycardia, asthma, HF	I
Verapamil	NA	1–2 h	120–360 mg daily in divided doses; slow release available	Hypotension, heart block, HF, digoxin interaction	I
Amiodarone	800 mg daily for 1 wk 600 mg daily for 1 wk 400 mg daily for 4–6 wk	1–3 wk	200 mg daily	Pulmonary toxicity, skin discoloration, hypothyroidism, corneal deposits, optic neuropathy, warfarin interaction, proarrhythmia	IIb

HF indicates heart failure; PO, by mouth; NA, not applicable; HF, heart failure; and BID, twice a day.
*Drugs are listed alphabetically within each class of recommendation.
**Recommended maintenance dosages are the usual ones necessary, but higher doses may be appropriate in some patients.
†The table includes representative members of the type of beta-blocker drugs, but other, similar agents could be used for this indication in appropriate doses.

with AF who experience symptoms related to a rapid ventricular rate during AF that cannot be adequately controlled with antiarrhythmic or negative chronotropic medications (83,84,86,163). AV nodal ablation is especially useful when an excessive ventricular rate induces a tachycardia-mediated decline in ventricular systolic function despite appropriate medical therapy.

The limitations of AV nodal ablation include the persistent need for anticoagulation, loss of AV synchrony, and lifelong pacemaker dependency. There is a small but real risk of sudden death, largely due to torsade de pointes (164). In addition, ablation of the AV conduction system might preclude or limit the later use of newer nonpharmacological treatments. Patients with impaired diastolic ventricular compliance who are most dependent on AV synchrony for maintenance of cardiac output (such as HCM or restrictive cardiomyopathies) might experience persistent symptoms after AV nodal ablation and permanent pacemaker implantation. Thus, patients must be counseled regarding each of these considerations before proceeding with this irreversible treatment.

The use of catheter ablation to modify AV nodal conduction by eliminating posterior atrial inputs to the AV node has been reported to decrease the ventricular rate during AF and to improve cardiac symptoms without requiring pacemaker implantation (165,166). This technique has several limitations, including the inadvertent induction of complete AV block and a relatively high risk of increasing ventricular rate over the first 6 months after ablation. Thus, AV nodal modification without pacemaker implantation is only rarely used for patients with rapid ventricular rates during AF.

G. Preventing Thromboembolism

1. Risk Stratification

a. Epidemiological Data

The rate of stroke in patients with AF is related to coexistent cardiovascular disease (4,19,73,74). In a small, retrospective, population-based study in Olmsted County, Minnesota, over 3 decades, the 15-year cumulative stroke rate in people with lone AF (defined as those younger than age 60 years with no clinical history or echocardiographic signs of cardiopulmonary disease) was 1.3% per year (4). Conversely, in the Framingham Study, the age-adjusted stroke rate over a mean follow-up period of 11 years was 28.2% in those with lone AF, which was more liberally defined to include patients with a history of hypertension or cardiomegaly on chest roentgenography; by comparison, the rate was 6.8% in normal controls. In the SPAF study, the annualized rate of ischemic stroke was similar in those with recurrent (3.2%) and permanent (3.3%) AF (167). Those with prior stroke or transient ischemic attack have a rate of subsequent stroke of 10% to 12% per year despite aspirin use and benefit substantially from treatment with adjusted-dose oral anticoagulation (168,169). In addition to prior thromboembolism, independent risk factors for ischemic stroke in nonvalvular AF include HF, hypertension, increasing age, and diabetes mellitus (19,73,170–172). Female sex, blood pressure greater than 160 mmHg, and LV dysfunction have each been linked to stroke (75,170,173). The relative risk for ischemic stroke associated with specific clinical features is given in Table 8. Nearly half of AF-associated strokes occur in patients greater than 75 years old, and AF is the most frequent cause of disabling stroke in elderly women (9,171,173). Older people are at increased risk for anticoagulant-related bleeding (174) and are therefore less likely to be treated with oral anticoagulation, even in situations for which it has been proven efficacious (175). Special consideration of the elderly is therefore warranted for effective stroke prophylaxis (171).

TABLE 8. Risk Factors for Ischemic Stroke and Systemic Embolism in Patients With Nonvalvular Atrial Fibrillation

Risk Factors (Control Groups)	Relative Risk
Previous stroke or TIA	2.5
History of hypertension	1.6
Congestive heart failure	1.4
Advanced age (continuous, per decade)	1.4
Diabetes mellitus	1.7
Coronary artery disease	1.5

TIA indicates transient ischemic attack. Relative risk refers to comparison with atrial fibrillation patients without these risk factors. As a group, patients with nonvalvular atrial fibrillation have about a 6-fold increased risk of thromboembolism compared with patients in normal sinus rhythm. Data from collaborative analysis of five primary prevention trials (75).

Patients with AF related to thyrotoxicosis, which is often associated with congestive HF, are also at increased risk for stroke (176–178), although the underlying mechanism is not clear (52,179,180). AF is a frequent complication of HCM (181), and such patients have an incidence of stroke and systemic embolism amounting to 2.4% to 7.1% per year (182–185).

b. Role of Echocardiography in Risk Stratification

Transthoracic Echocardiography: In a meta-analysis of 3 randomized trials of antithrombotic therapy, moderate to severe LV dysfunction was the only independent echocardiographic predictor of stroke in patients with AF when clinical features were also considered (186). The diameter of the LA was a less useful predictor of ischemic events (186). Transthoracic Echocardiography TEE is the most sensitive and specific imaging technique for detection of LA and LA appendage (LAA) thrombus, far surpassing transthoracic echocardiography (52). This modality also permits superior evaluation for other causes of cardiogenic embolism (187) and superiority in measuring LAA function (188). Several TEE features have been associated with thromboembolism, including such LA/LAA abnormalities as thrombus, reduced flow velocity, and spontaneous echo contrast, as well as complex atheromatous plaques in the aorta (70,189).

Detection of LA/LAA thrombus stands as a contraindication to elective cardioversion of AF. The absence of detectable thrombus does not preclude thromboembolism after cardioversion if patients do not receive anticoagulation therapy (190,191). A TEE-guided strategy for elective cardioversion of AF has been reported to result in comparable outcomes for thromboembolism and death compared with conventional anticoagulation for 3 weeks before and 4 weeks after cardioversion (192). Hence, transthoracic echocardiog-

TABLE 9. Published Risk-Stratification Schemes for Primary* Prevention of Thromboembolism in Patients With Nonvalvular Atrial Fibrillation

Source	High Risk	Intermediate Risk	Low Risk
Atrial Fibrillation Investigators (194)†	Age greater than or equal to 65 years History of hypertension Coronary artery disease Diabetes		Age less than 65 years No high-risk features
American College of Chest Physicians (193)	Age greater than 75 years History of hypertension Left ventricular dysfunction‡ More than 1 intermediate risk factor	Age 65–75 years Diabetes Coronary artery disease Thyrotoxicosis	Age less than 65 years No risk factors
Stroke Prevention in Atrial Fibrillation (186)	Women greater than 75 years Systolic BP greater than 160 mm Hg Left ventricular dysfunction†	History of hypertension No high-risk features	No high-risk features No history of hypertension

BP indicates blood pressure. Patients are classified on the basis of the presence or absence of any risk factor.

Adapted with permission from Am J Med, Vol. 109, Pearce et al., Assessment of these schemes for stratifying stroke risk in patients with nonvalvular atrial fibrillation, pp. 45–51, © 2000, with permission, from Excerpta Medica, Inc. (195).

*Patients with AF and prior thromboembolism are at high risk of stroke, and anticoagulation is indicated for secondary prevention in such cases.

†Did not distinguish high-risk from intermediate-risk patients.

‡Left ventricular dysfunction refers to moderate to severe wall motion abnormality assessed globally by 2-dimensional echocardiography, reduced ejection fraction, fractional shortening less than 0.25 by M-mode echocardiography, or clinical heart failure.

raphy is valuable for defining the origin of AF (eg, to detect rheumatic mitral valve disease or HCM), and TEE can provide additional information for stratifying thromboembolic risk. Three clinical schemes have been proposed recently to stratify the risk of ischemic stroke in AF patients that are directly or indirectly based on analyses of prospectively monitored cohorts of participants in clinical trials in which antithrombotic therapy was controlled (172,186,193). One set of criteria is based on multivariate pooled analysis of 1593 participants assigned to the control or placebo groups of 5 randomized primary prevention trials in which 106 ischemic strokes occurred over a mean follow-up of 1.4 years (19). This scheme divides patients into 2 strata, distinguishing low-risk patients from those at intermediate or high risk. Echocardiographic features were not considered initially, but subsequent analysis of 3 of these trials identified abnormal LV systolic function as an independent predictor of stroke (186). The SPAF study criteria were based on multivariate analysis of 854 participants assigned aspirin in the SPAF-I and -II clinical trials who were followed up for a mean of 2.3 years, during which 68 ischemic strokes were observed. A third set of criteria was developed by expert consensus (193) based on consideration of the 2 foregoing schemes and other available data to classify patients into low-, intermediate-, and high-risk groups (Table 9).

c. Therapeutic Implications

The risk of thromboembolism for patients with chronic atrial flutter is generally estimated as higher than for patients with sinus rhythm but less than for those with persistent or permanent AF. Biblo et al. (196) recently reviewed 8 years of retrospective data on 749,988 hospitalized older patients, including 17,413 with atrial flutter and 337,428 with AF. The overall stroke risk ratio for patients with atrial flutter was 1.4 compared with the control group; for patients with AF, the relative risk was 1.6. As a chronic arrhythmia, atrial flutter is uncommon, and the risk of thromboembolism is not as well established as it is for AF. Until more robust data become available, and although the overall thromboembolic risk associated with atrial flutter can be lower than with AF, it seems prudent to estimate risk by use of similar stratification criteria.

2. Antithrombotic Strategies for Prevention of Ischemic Stroke and Systemic Embolism

Five large randomized trials published between 1989 and 1992 evaluated oral anticoagulation, and 2 tested aspirin for primary prevention of thromboembolism in patients with nonvalvular AF (24,197–199). A sixth trial focused on secondary prevention among patients who had survived nondisabling stroke or transient cerebral ischemic attack (169). Meta-analysis according to the principle of intention to treat showed that adjusted-dose oral anticoagulation is highly efficacious for prevention of all stroke (both ischemic and hemorrhagic), with a risk reduction of 61% (95% CI 47% to 71%) vs placebo (200) (Fig. 6). This reduction was similar for both primary and secondary prevention. The duration of follow-up in these trials was generally between 1 and 2 years; the longest was 2.2 years, whereas in clinical practice, the need for antithrombotic therapy typically extends over much longer periods.

Patient age and the intensity of anticoagulation are the most powerful predictors of major bleeding (201–204). Trial participants, at an average age of 69 years, were carefully selected and managed. It is thus unclear whether the relatively low rates of major hemorrhage also apply to AF patients in clinical practice, who have a mean age of approximately 75 years and whose anticoagulation therapy is less closely regulated (205,206).

The target intensity of anticoagulation involves a balance between prevention of ischemic stroke and avoidance of hemorrhagic complications. It is important to target the lowest adequate intensity of anticoagulation to minimize the risk of bleeding, particularly for elderly AF patients. Maxi-

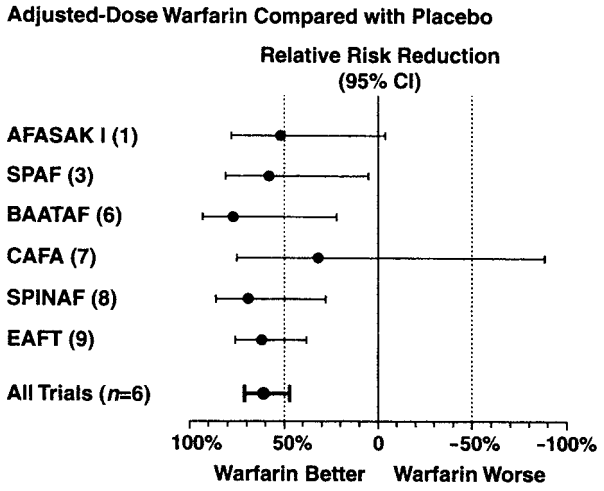

Figure 6. Antithrombotic therapy for prevention of stroke (ischemic and hemorrhagic) in patients with nonvalvular AF: adjusted-dose warfarin compared with placebo. Adapted with permission from Hart et al. (170,200) Ann Intern Med 1999;131:492–501. (The American College of Physicians–American Society of Internal Medicine is not responsible for the accuracy of the translation.)

mum protection against ischemic stroke in AF is probably achieved with an international normalized ratio (INR) of 2 to 3 (168,207,208), whereas an INR range of 1.6 to 2.5 appears to be associated with incomplete efficacy, estimated at approximately 80% of that achieved with higher intensity anticoagulation (Fig. 7) (207,209).

In patients with AF who do not have mechanical valves, it is the consensus of the writing group that anticoagulation can be interrupted for a period of up to 1 week for procedures that carry a risk of bleeding, without substituting heparin. In high-risk patients, or when a series of procedures requires interruption for a period longer than 1 week, unfractionated or low-molecular-weight heparin can be administered intravenously or subcutaneously, respectively.

Low-molecular-weight heparins have several pharmacological advantages over unfractionated heparin. These include a longer half-life, more predictable bioavailability (greater than 90% after subcutaneous injection), predictable clearance (enabling once- or twice-daily subcutaneous administration), and predictable antithrombotic response based on body weight, which permits fixed-dose treatment without laboratory monitoring except under special circumstances, such as obesity, renal insufficiency, or pregnancy (210). Low-molecular-weight heparins carry a lower risk of heparin-induced thrombocytopenia than unfractionated heparin (211). Self-administration of low-molecular-weight heparins out of hospital is a promising approach that can result in cost savings in conjunction with elective cardioversion (212).

Aspirin offers only modest protection against stroke for patients with AF (Fig. 8). The effect is less consistent than that of oral anticoagulation (200,213). Aspirin might be more efficacious for AF patients with hypertension or diabetes (213,214) and for reducing noncardioembolic versus cardioembolic ischemic strokes (49). Cardioembolic strokes are, on average, more disabling than noncardioembolic strokes (69).

3. Conversion to Sinus Rhythm and Thromboembolism

Randomized studies of antithrombotic therapy are lacking for patients undergoing cardioversion of AF or atrial flutter, but the risk of thromboembolism was between 1% and 5% in case-control series (102,215). There is no solid clinical evidence that cardioversion of AF followed by prolonged maintenance of sinus rhythm effectively reduces thromboembolism. Patients in whom LAA thrombus is identified by TEE appear to be at high risk of thromboembolism after cardioversion of AF or flutter, and they should be treated with anticoagulation for at least 3 to 4 weeks before and after either pharmacological or electrical cardioversion.

In a multicenter study (192), 1222 patients with either AF persisting longer than 2 days or atrial flutter and previous AF were randomized to a TEE-guided or conventional strategy. One group received anticoagulation with heparin just before

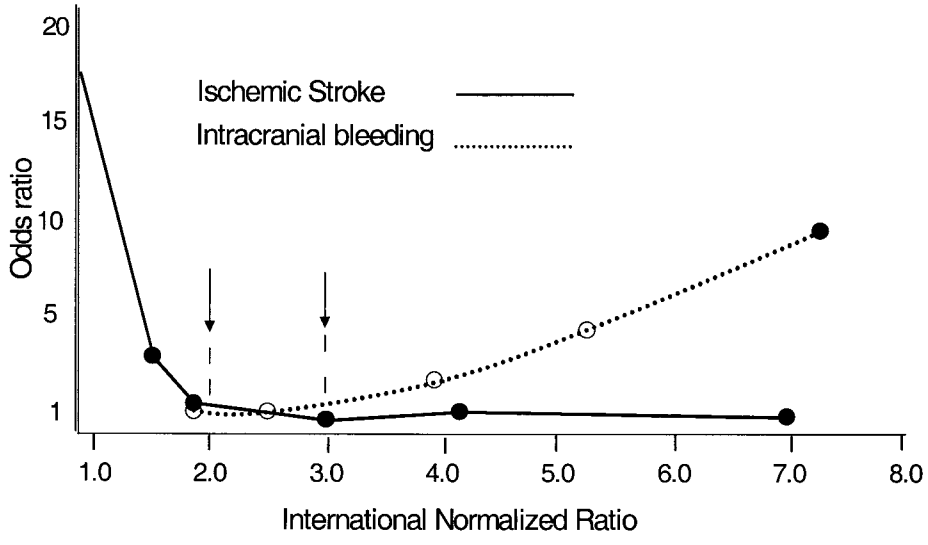

Figure 7. Adjusted odds ratios for ischemic stroke and intracranial bleeding in relation to intensity of anticoagulation in randomized trials of antithrombotic therapy for patients with AF. The data are from Hylek et al (203,207).

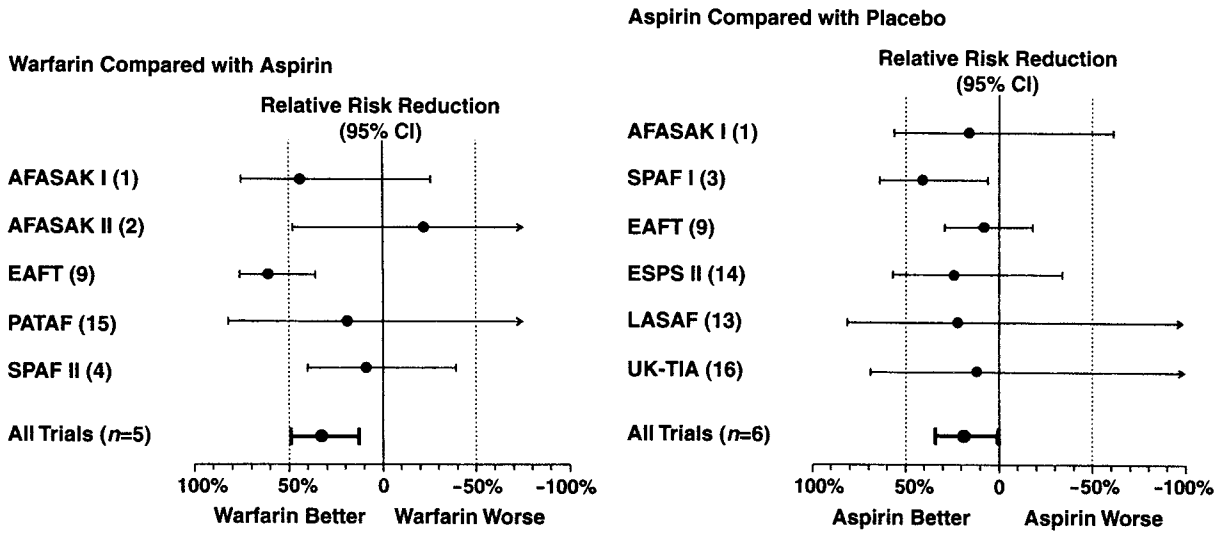

Figure 8. Antithrombotic therapy for prevention of stroke (ischemic and hemorrhagic) in patients with nonvalvular AF: warfarin compared with aspirin and aspirin compared with placebo. Adapted with permission from Hart et al. (170,200) Ann Intern Med 1999;131:492–501. (The American College of Physicians–American Society of Internal Medicine is not responsible for the accuracy of the translation.)

and with warfarin for 4 weeks after cardioversion. When thrombus was identified, cardioversion was postponed, and warfarin was administered for 3 weeks before TEE was repeated. The other group received anticoagulant therapy for 3 weeks before and 4 weeks after cardioversion. Both approaches were associated with a comparably low risk of stroke (0.8% with the TEE-guided approach and 0.5% with the conventional approach) after 8 weeks of follow-up. The risk of major bleeding did not differ significantly. There were no differences in the proportion of subjects in whom sinus rhythm was successfully restored. Thus, the clinical benefit of the TEE approach was limited to saving time before cardioversion.

Conversion of AF to sinus rhythm results in transient mechanical dysfunction of the LA and LAA (190), known as "stunning." This occurs after spontaneous, pharmacological (216,217), or electrical (217–219) conversion of AF and after radiofrequency catheter ablation of atrial flutter (220). The loss of atrial function can be associated with spontaneous echo contrast (190). Recovery of mechanical function can be delayed for several weeks, depending in part on the duration of AF before restoration of sinus rhythm (221–223). This could explain why some patients with no demonstrable LA thrombus on TEE before cardioversion subsequently experience thromboembolic events (191). Presumably, thrombus forms during the period of stunning and is expelled after the return of mechanical function, which explains the clustering of thromboembolic events in the first 10 days after cardioversion (224).

Anticoagulation is recommended for 3 to 4 weeks before and after cardioversion for patients with AF of unknown duration or that has lasted more than 48 h. Although LA thrombus and systemic embolism have been documented in patients with AF of shorter duration, the need for anticoagulation in such patients is less clear. When acute AF produces hemodynamic instability, immediate cardioversion should not be delayed, but intravenous heparin or low-molecular-weight heparin should be administered first. Protection against late embolism might require continuation of anticoagulation; the duration of anticoagulation after the procedure depends on the likelihood that AF will recur and on the patient's intrinsic risk of thromboembolism.

IX. Proposed Management Strategies

A. Overview of Algorithms for Management of Patients With AF

Management of patients with AF requires knowledge of its pattern of presentation (paroxysmal, persistent, or permanent) and decisions about restoration and maintenance of sinus rhythm, control of the ventricular rate, and anticoagulation. These issues are addressed in the various management algorithms for each presentation of AF.

1. Newly Discovered or First Episode of AF (Fig. 9)

It is not always clear whether the initial presentation of AF is actually the patient's first episode, particularly in those with minimal or no symptoms of the dysrhythmia, so both are considered together. In patients who have self-limited episodes of paroxysmal AF, antiarrhythmic drugs to prevent recurrence are usually unnecessary, unless AF is associated with severe symptoms related to hypotension, myocardial ischemia, or HF. Whether these individuals require long-term or even short-term anticoagulation is not clear, and the decision must be individualized for each patient based on the intrinsic risk of thromboembolism.

In patients with persistent AF, one option is to accept progression to permanent AF, with attention to antithrombotic therapy and control of the ventricular rate. Although it might seem reasonable to make at least 1 attempt to restore sinus rhythm, this is not in the best interest of all patients. An example is the older man without risk factors for thromboembolism in whom asymptomatic AF is discovered on routine examination and control of the ventricular rate is

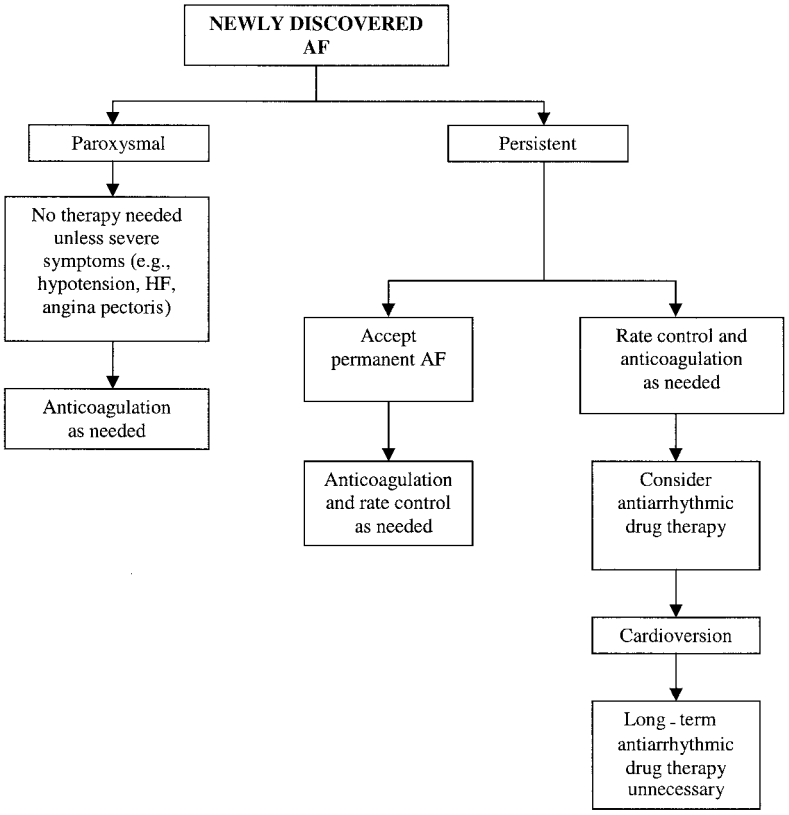

Figure 9. Pharmacological management of patients with newly discovered AF. AF indicates atrial fibrillation; HF, heart failure.

readily achieved. Here, the potential toxicity of antiarrhythmic drugs might outweigh the benefit of restoration of sinus rhythm. If the decision is made to attempt to restore and maintain sinus rhythm, anticoagulation and rate control are important before cardioversion. Although long-term antiarrhythmic therapy might not be needed to prevent recurrent AF after cardioversion, short-term therapy might be beneficial. In patients with AF of more than 3 months' duration, early recurrence is common after cardioversion. Antiarrhythmic medication can be initiated before cardioversion (after adequate anticoagulation) in such cases to reduce the likelihood of recurrence, and the duration of drug therapy would be brief (eg, 1 month).

2. Recurrent Paroxysmal AF (Fig. 10 and 11)

In patients who experience brief or minimally symptomatic recurrences of paroxysmal AF, it is reasonable to avoid antiarrhythmic drugs, but troublesome symptoms generally call for suppressive antiarrhythmic therapy. Rate control and prevention of thromboembolism are appropriate in both situations. In any given patient, several different antiarrhythmic drugs might be effective, and the initial selection is thus based mainly on safety. For individuals with no or minimal structural heart disease, flecainide, propafenone, and sotalol are recommended as initial antiarrhythmic therapy because they are generally well tolerated and are essentially devoid of extracardiac organ toxicity. When one or another of these drugs is ineffective or is associated with side effects, then second or third line choices include amiodarone, disopyramide, procainamide, and quinidine, which have greater potential for adverse reactions. A nonpharmacological approach is appropriate for some patients, and this should be considered before amiodarone therapy is begun. Occasionally, a consistent initiating factor can be found. Disopyramide or flecainide may be used in cases of vagally mediated AF, whereas beta-blockers or sotalol is suggested as the initial agent for adrenergically induced AF.

Many patients with organic heart disease can be broadly categorized into those with HF, CAD, or hypertension, although other types of heart disease can also be associated with AF. For patients with HF, safety data support the selection of amiodarone or dofetilide to maintain sinus rhythm. Patients with ischemic heart disease often require beta-blocker medication. Then sotalol, a drug with both beta-blocking activity and primary antiarrhythmic efficacy, is considered first unless the patient has HF. Amiodarone and dofetilide are considered secondary agents in this situation. The clinician may consider disopyramide, procainamide, or quinidine on an individual basis. In patients with hypertension without LVH, drugs such as flecainide and propafenone, which do not prolong repolarization and the QT interval, might offer a safety advantage and are recommended first. If these agents either prove ineffective or produce side effects, then amiodarone, dofetilide, and sotalol represent appropriate secondary choices. Disopyramide, procainamide, and quinidine are considered third-line agents in this situation. Hypertrophied myocardium is prone to proarrhythmic toxicity and development of the torsade de pointes type of ventricular tachycardia. Amiodarone is suggested as first-line therapy in patients with LVH (wall thickness greater than or equal to

1.4 cm) on the basis of its relative safety compared with several other agents. Because neither ECG nor echocardiography invariably detects LVH as defined by measurement of myocardial mass, clinicians face a conundrum. The selection of antiarrhythmic drugs for patients with a history of hypertension is compounded by the dearth of prospective controlled trials comparing the safety and efficacy of drug therapy for AF.

The scarcity of data from randomized trials of antiarrhythmic medications for treatment of patients with AF applies generally to all patient groups. Accordingly, the drug-selection algorithm presented here has been developed as a consensus of experts and is particularly subject to revision as additional evidence emerges in this field (Fig. 10).

3. Recurrent Persistent AF (Fig. 11 and 12)

Patients with minimal symptoms who have undergone at least 1 attempt to restore sinus rhythm can remain in AF with therapy for rate control and prevention of thromboembolism. Alternatively, those with symptoms favoring sinus rhythm should be treated with an antiarrhythmic agent (in addition to medications for rate control and anticoagulation) before cardioversion. The selection of an antiarrhythmic drug should be based on the same algorithm used for patients with recurrent paroxysmal AF.

4. Permanent AF (Fig. 12)

Permanent AF is the designation given to cases in which sinus rhythm cannot be sustained after cardioversion of AF or when the patient and physician have decided to allow AF to continue without further efforts to restore sinus rhythm. It is important to maintain control of the ventricular rate and to use antithrombotic therapy, as outlined elsewhere in this document, for all patients in this category.

B. Recommendations for Management of Patients With AF

Recommendations are evidence based and are derived primarily from published data. The weight of evidence was ranked highest (A) when the data were derived from multiple randomized clinical trials and intermediate (B) when the data were derived from a limited number of randomized trials, nonrandomized studies, or observational registries. A lower rank (C) was given when the primary basis for the recommendation was expert consensus.

Recommendations follow the format of previous ACC/AHA guidelines for classifying indications, summarizing both the evidence and expert opinion:

Class I: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: The weight of evidence or opinion is in favor of the procedure or treatment.

Class IIb: Usefulness/efficacy is less well established by evidence or opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases can be harmful.

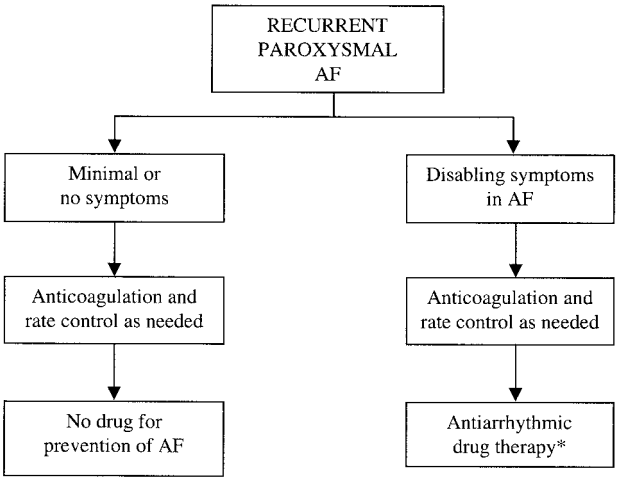

Figure 10. Pharmacological management of patients with recurrent paroxysmal AF. *See Figure 11 for suggested drugs.

The reader is referred to the full-text guidelines available on the ACC (www.acc.org), AHA (www.americanheart.org), ESC (www.escardio.org), and NASPE (www.naspe.org) World Wide Web sites and published in the European Heart Journal in mid-October 2001 for a complete description of the rationale and evidence supporting these recommendations.

Recommendations for Pharmacological and Electrical Cardioversion of AF

Class I

1. **Immediate electrical cardioversion in patients with paroxysmal AF and a rapid ventricular response who have ECG evidence of acute MI or symptomatic hypotension, angina, or HF that does not respond promptly to pharmacological measures. (*Level of Evidence: C*)**
2. **Cardioversion in patients without hemodynamic instability when symptoms of AF are unacceptable. (*Level of Evidence: C*)**

Class IIa

1. **Pharmacological or electrical cardioversion to accelerate restoration of sinus rhythm in patients with a first-detected episode of AF. (*Level of Evidence: C*) (See Tables 10 through 12 for recommended drugs.)**
2. **Electrical cardioversion in patients with persistent AF when early recurrence is unlikely. (*Level of Evidence: C*)**
3. **Repeated cardioversion followed by prophylactic drug therapy in patients who relapse to AF without antiarrhythmic medication after successful cardioversion. (*Level of Evidence: C*)**

Class IIb

1. **Pharmacological agents for cardioversion to sinus rhythm in patients with persistent AF. (*Level of Evidence: C*) (See Tables 10 through 12 for recommended drugs.)**

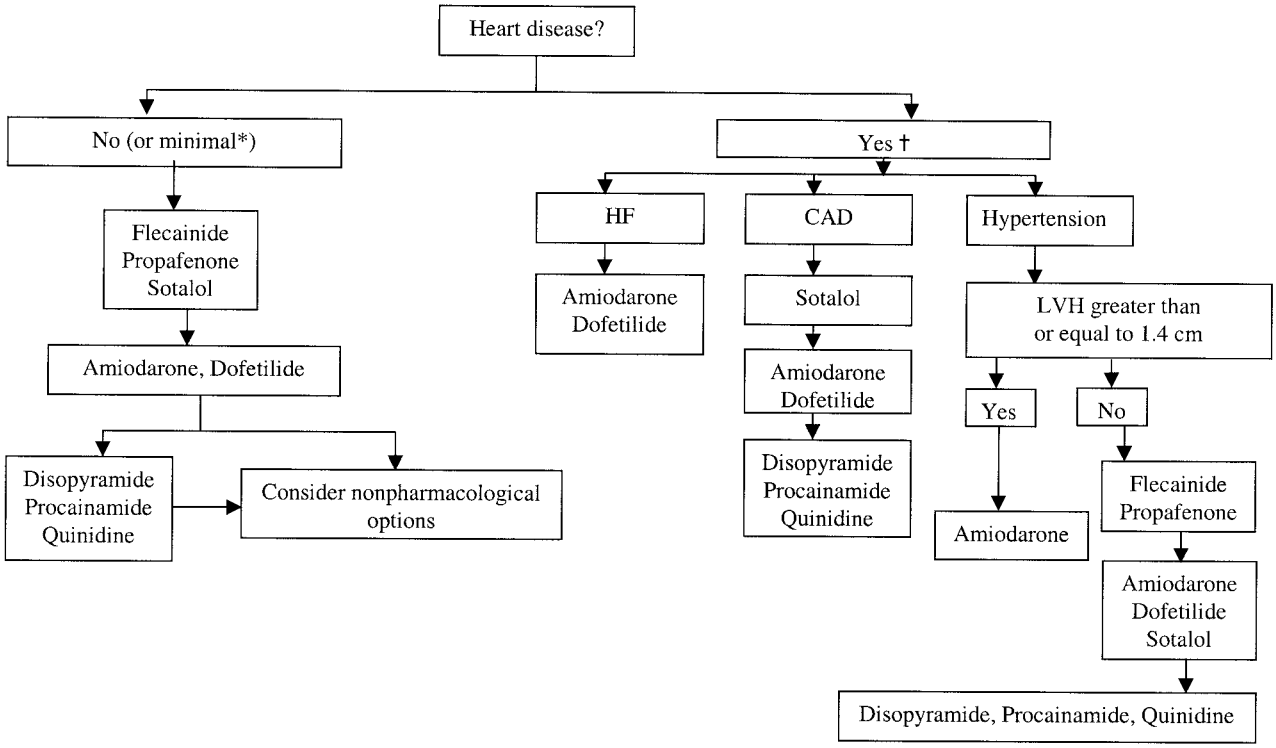

Figure 11. Antiarrhythmic drug therapy to maintain sinus rhythm in patients with recurrent paroxysmal or persistent atrial fibrillation. Drugs are listed alphabetically and not in order of suggested use. *For adrenergic atrial fibrillation, beta-blockers or sotalol are the initial drugs of choice. †Consider nonpharmacological options to maintain sinus rhythm if drug failure occurs. HF indicates heart failure; CAD, coronary artery disease; and LVH, left ventricular hypertrophy.

2. **Out-of-hospital administration of pharmacological agents for cardioversion of first-detected, paroxysmal, or persistent AF in patients without heart disease or when the safety of the drug in the particular patient has been verified. (*Level of Evidence: C*) (See Table 12.)**

Class III

1. **Electrical cardioversion in patients who display spontaneous alternation between AF and sinus rhythm over short periods of time. (*Level of Evidence: C*)**

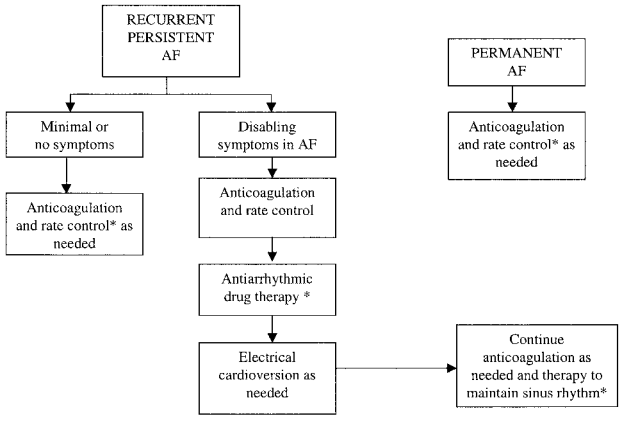

Figure 12. Pharmacological management of patients with recurrent persistent or permanent AF. *See Fig. 11. Initiate drug therapy before cardioversion to reduce the likelihood of early recurrence of AF.

2. **Additional cardioversion in patients with short periods of sinus rhythm who relapse to AF despite multiple cardioversion procedures and prophylactic antiarrhythmic drug treatment. (*Level of Evidence: C*)**

Recommendations for Pharmacological Therapy to Maintain Sinus Rhythm (See Table 3)

Pharmacological management strategies or algorithms to maintain sinus rhythm in patients with AF (Figs. 9, 10, 11, 12) are based on available evidence and extrapolated from experience with these agents in other situations.

Class I

1. **Base selection of pharmacological therapy to maintain sinus rhythm in patients with disabling or otherwise troublesome symptoms during AF predominantly on safety. (*Level of Evidence: B*)**
2. **Treat precipitating or reversible causes of AF before initiating antiarrhythmic drug therapy. (*Level of Evidence: C*)**

Class IIa

1. **Administer pharmacological therapy to maintain sinus rhythm to prevent progression of tachycardia-induced cardiomyopathy due to AF. (*Level of Evidence: C*)**
2. **Infrequent and well-tolerated recurrence of AF may in some cases be deemed a successful outcome of antiarrhythmic drug therapy. (*Level of Evidence: C*)**

TABLE 10. Recommendations for Pharmacological Cardioversion of AF Less Than or Equal to 7 Days Duration**

Drug*	Route of Administration	Type of Recommendation	Level of Evidence	References
Agents with proven efficacy				
Dofetilide	Oral	I	A	133, 225–229
Flecainide	Oral or intravenous	I	A	88–90, 92, 230–235
Ibutilide	Intravenous	I	A	236–241
Propafenone	Oral or intravenous	I	A	90, 93, 94, 230, 233, 235, 242–252
Amiodarone	Oral or intravenous	IIa	A	92, 96, 124, 234, 251, 253–260
Quinidine	Oral	IIb	B	88, 90, 91, 93, 242, 256, 257, 261, 262
Less effective or incompletely studied agents				
Procainamide	Intravenous	IIb	C	237, 238, 263
Digoxin	Oral or intravenous	III	A	93, 233, 244, 259, 264–267
Sotalol	Oral or intravenous	III	A	239, 261, 262, 266, 268

*Drugs are listed alphabetically within each category of recommendation and level of evidence.
**The doses of medications used in these studies may not be the same as those recommended by the manufacturers.

3. **Outpatient initiation of antiarrhythmic drug treatment is appropriate in selected patients. (*Level of Evidence: C*)**

Class IIb

1. **Administer pharmacological therapy to maintain sinus rhythm in asymptomatic patients to prevent atrial remodeling. (*Level of Evidence: C*)**
2. **Administer pharmacological therapy to maintain sinus rhythm to prevent thromboembolism or HF in selected patients. (*Level of Evidence: C*)**
3. **Administer combinations of antiarrhythmic agents to maintain sinus rhythm when single-drug therapy fails. (*Level of Evidence: C*)**

Class III

1. **Use of a particular pharmacological agent to maintain sinus rhythm in patients with well-defined proarrhythmia risk factors for that agent. (*Level of Evidence: A*)**
2. **Use of pharmacological therapy to maintain sinus rhythm in patients with advanced sinus node or AV node dysfunction in the absence of a functioning electronic cardiac pacemaker. (*Level of Evidence: C*)**

Recommendations for Heart Rate Control in Patients With AF (See Tables 6, 7, and 13)

Class I

1. **Measure heart rate response both at rest and during exercise in patients with persistent or permanent AF and control the rate with pharmacological agents (using a beta-blocker or calcium channel antagonist in most cases) to the physiological range. (*Level of Evidence: C*)**
2. **Administer intravenous beta-blockers or calcium channel antagonists (verapamil, diltiazem) in the acute setting to slow the ventricular response to AF in the absence of conduction over an accessory pathway, exercising caution in patients with hypotension or HF. (*Level of Evidence: B*)**
3. **Perform immediate electrical cardioversion in patients with acute paroxysmal AF and a rapid ventricular response associated with acute myocardial infarction, symptomatic hypotension, angina, or cardiac**

TABLE 11. Recommendations for Pharmacological Cardioversion of AF More Than 7 Days Duration**

Drug*	Route of Administration	Type of Recommendation	Level of Evidence	References
Agents proven effective				
Dofetilide	Oral	I	A	133, 225–229
Amiodarone	Oral or intravenous	IIa	A	92, 96, 124, 234, 251, 253–260
Ibutilide	Intravenous	IIa	A	236–241
Flecainide	Oral	IIb	B	88–90, 92, 230–235
Propafenone	Oral or intravenous	IIb	B	90, 93, 94, 230, 233, 235, 242–252
Quinidine	Oral	IIb	B	88, 90, 91, 93, 242, 256, 257, 261, 262
Less effective or incompletely studied agents				
Procainamide	Intravenous	IIb	C	237, 238, 263
Sotalol	Oral or intravenous	III	A	239, 261, 262, 266, 268
Digoxin	Oral or intravenous	III	C	93, 233, 244, 259, 264–267

*Drugs are listed alphabetically within each category of recommendation and level of evidence.
**The doses of medications used in these studies may not be the same as those recommended in Table 3 or by the manufacturers.

failure that does not respond promptly to pharmacological measures. (*Level of Evidence: C*)

Class IIa
1. Administer a combination of digoxin and a beta-blocker or calcium channel antagonist to control the heart rate at rest and during exercise in patients with AF. The choice of medication should be individualized and the dose modulated to avoid bradycardia. (*Level of Evidence: C*)
2. Employ nonpharmacological therapy to control heart rate when pharmacological therapy is insufficient. (*Level of Evidence: C*)

Class IIb
1. Administer digoxin as the sole agent to control heart rate at rest in patients with persistent AF. (*Level of Evidence: B*)
2. Administer intravenous quinidine, procainamide, disopyramide, ibutilide, or amiodarone to hemodynamically stable patients with AF involving conduction over an accessory pathway. (*Level of Evidence: B*)
3. Immediate cardioversion is required when very rapid tachycardias or hemodynamic instability occurs in patients with AF involving conduction over an accessory pathway. (*Level of Evidence: B*)

Class III
1. Administer digitalis as the sole agent to control a rapid rate of ventricular response to AF in patients with paroxysmal AF. (*Level of Evidence: B*)
2. Catheter ablation without prior medical therapy to control AF. (*Level of Evidence: C*)

Recommendations for Antithrombotic Therapy in Patients With AF (see Table 14)

Class I
1. Administer antithrombotic therapy (oral anticoagulation or aspirin) to all patients with AF, except those with lone AF, to prevent thromboembolism. (*Level of Evidence: A*)
2. Individualize the selection of the antithrombotic agent based on assessment of the absolute risks of stroke and bleeding and the relative risk and benefit for a particular patient. (*Level of Evidence: A*)
3. Chronic oral anticoagulant therapy in a dose adjusted to achieve a target intensity of INR 2 to 3 in patients at high risk of stroke, unless contraindicated. (*Level of Evidence: A*)
   a. The need for anticoagulation should be reevaluated at regular intervals. (*Level of Evidence: A*)
   b. INR should be determined at least weekly during the initiation of oral anticoagulation therapy and monthly when the patient is stable. (*Level of Evidence: A*)
4. Aspirin in a dose of 325 mg daily as an alternative in low-risk patients or in those with certain contraindications to oral anticoagulation. (*Level of Evidence: A*)
5. Oral anticoagulation for patients with AF who have rheumatic mitral valve disease or prosthetic heart valves (mechanical or tissue valves). (*Level of Evidence: B*)
   a. Base the target intensity of anticoagulation on the particular type of prosthesis, but it should not be less than INR 2 to 3. (*Level of Evidence: B*)

Class IIa
1. Target a lower INR of 2 (range 1.6 to 2.5) for primary prevention of ischemic stroke and systemic embolism in patients over 75 years old considered at increased risk of bleeding complications but without frank contraindications to oral anticoagulant therapy. (*Level of Evidence: C*)
2. Manage antithrombotic therapy for patients with atrial flutter, in general, as for those with AF. (*Level of Evidence: C*)
3. Select antithrombotic therapy by the same criteria irrespective of the pattern of AF (ie, for patients with paroxysmal, persistent, or permanent AF). (*Level of Evidence: B*)

Class IIb
1. Interrupt anticoagulation for a period of up to 1 week for surgical or diagnostic procedures that carry a risk of bleeding, without substituting heparin in patients with AF who do not have mechanical prosthetic heart valves. (*Level of Evidence: C*)
2. Administer unfractionated or low-molecular-weight heparin intravenously or subcutaneously, respectively in selected high-risk patients or when a series of procedures requires interruption of oral anticoagulant therapy for a period longer than 1 week. (*Level of Evidence: C*)
3. Manage patients with CAD with anticoagulation (INR 2 to 3) based on the same criteria used for patients without CAD. (*Level of Evidence: C*)
   a. A low dose of aspirin (less than 100 mg per day) or clopidogrel (75 mg per day) may be given concurrently with anticoagulation, but these strategies have not been evaluated sufficiently and may be associated with an increased risk of bleeding. (*Level of Evidence: C*)
4. Treatment with aspirin is optional for primary prevention of stroke in patients under age 60 years without heart disease or risk factors for thromboembolism (lone AF). (*Level of Evidence: C*)

Class III

Long-term anticoagulation for stroke prevention in patients under 60 years of age without heart disease (lone AF) and without risk factors for thromboembolism. (*Level of Evidence: C*)

Recommendations for Antithrombotic Therapy to Prevent Ischemic Stroke and Systemic Embolism in Patients With AF Undergoing Cardioversion

Class I
1. Administer anticoagulation therapy regardless of the method (electrical or pharmacological) used to restore sinus rhythm. (*Level of Evidence: B*)
2. Anticoagulate patients with AF lasting more than 48 h or of unknown duration for at least 3 to 4 weeks

TABLE 12. Recommended Doses of Drugs Proven Effective for Pharmacological Cardioversion of Atrial Fibrillation

Drug*	Route of Administration	Dosage**	Potential Adverse Effects	References
Amiodarone	Oral	Inpatient: 1.2–1.8 g per day in divided dose until 10 g total, then 200–400 mg per day maintenance or 30 mg/kg as single dose	Hypotension, bradycardia, QT prolongation, torsade de pointes (rare), GI upset, constipation, phlebitis (IV)	92, 96, 124, 234, 251, 253–260
		Outpatient: 600–800 mg per day divided dose until 10 g total, then 200–400 mg per day maintenance		
	Intravenous/oral	5–7 mg/kg over 30–60 min, then 1.2–1.8 g per day continuous IV or in divided oral doses until 10 g total, then 200–400 mg per day maintenance		
Dofetilide	Oral	Creatinine clearance (mL/min) / Dose (mcg BID): greater than 60 / 500; 40–60 / 250; 20–40 / 125; less than 20 / Contraindicated	QT prolongation, torsade de pointes; adjust dose for renal function, body size, and age	133, 225–229
Flecainide	Oral	200–300 mg†	Hypotension, rapidly conducting atrial flutter	88–90, 92, 230–235
	Intravenous	1.5–3.0 mg per kg over 10–20 min†		
Ibutilide	Intravenous	1 mg over 10 min; repeat 1 mg when necessary	QT prolongation, torsade de pointes	236–241
Propafenone	Oral	450–600 mg	Hypotension, rapidly conducting atrial flutter	90, 93, 94, 230, 233, 235, 242–252
	Intravenous	1.5–2.0 mg per kg over 10–20 min†		
Quinidine‡	Oral	0.75–1.5 g in divided doses over 6–12 h, usually with a rate-slowing drug	QT prolongation, torsade de pointes, GI upset, hypotension	88, 90, 91, 93, 242, 256, 257, 261, 262

GI indicates gastrointestinal; IV, intravenous; BID, twice a day.

*Drugs are listed alphabetically.

**Dosages given in the table may differ from those recommended by the manufacturers.

†Insufficient data are available on which to base specific recommendations for the use of one loading regimen over another for patients with ischemic heart disease or impaired left ventricular function, and these drugs should be used cautiously or not at all in such patients.

‡The use of quinidine loading to achieve pharmacological conversion of atrial fibrillation is controversial, and safer methods are available with the alternative agents listed in the table. Quinidine should be used with caution.

before and after cardioversion (INR 2 to 3). (*Level of Evidence: B*)

3. Perform immediate cardioversion in patients with acute (recent-onset) AF accompanied by symptoms or signs of hemodynamic instability resulting in angina pectoris, myocardial infarction, shock, or pulmonary edema, without waiting for prior anticoagulation. (*Level of Evidence: C*)

a. If not contraindicated, administer heparin concurrently by an initial intravenous bolus injection followed by a continuous infusion in a dose adjusted to prolong the activated partial thromboplastin time at 1.5 to 2 times the reference control value.

b. Next, provide oral anticoagulation (INR 2 to 3) for a period of at least 3 to 4 weeks, as for patients undergoing elective cardioversion. (*Level of Evidence: C*)

c. Limited data from recent studies support subcutaneous administration of low-molecular-weight heparin in this indication. (*Level of Evidence: C*)

4. Screening for the presence of thrombus in the LA or LAA by TEE is an alternative to routine preanticoagulation in candidates for cardioversion of AF. (*Level of Evidence: B*)

TABLE 13. Recommendations for Use of Pharmacological Agents to Control the Rate of Ventricular Responses to Atrial Fibrillation

Drug*	Route of Administration	Type of Recommendation	Level of Evidence
Diltiazem	Intravenous	I	A
Esmolol	Intravenous	I	A
Verapamil	Intravenous or oral	I	A
Other beta-blockers	Intravenous or oral	I	B
Digoxin	Intravenous or oral	IIa	B

*The doses of medications used in these studies may not be the same as those recommended by the manufacturers.

TABLE 14. Recommendations for Antithrombotic Therapy in Patients With Atrial Fibrillation Based on Thromboembolic Risk Stratification

Patient Features	Antithrombotic Therapy	Grade of Recommendation
Age less than 60 years No heart disease (lone AF)	Aspirin (325 mg daily) or no therapy	I
Age less than 60 years Heart disease but no risk factors*	Aspirin (325 mg daily)	I
Age greater than or equal to 60 years No risk factors*	Aspirin (325 mg daily)	I
Age greater than or equal to 60 years With diabetes mellitus or CAD	Oral anticoagulation (INR 2.0–3.0)	I
	Addition of aspirin, 81–162 mg daily is optional	IIb
Age greater than or equal to 75 years especially women	Oral anticoagulation (INR ≈2.0)	I
HF LV ejection fraction less than or equal to 0.35 Thyrotoxicosis Hypertension	Oral anticoagulation (INR 2.0–3.0)	I
Rheumatic heart disease (mitral stenosis) Prosthetic heart valves Prior thromboembolism Persistent atrial thrombus on TEE	Oral anticoagulation (INR 2.5–3.5 or higher may be appropriate)	I

*Risk factors for thromboembolism include HF, LV ejection fraction less than 0.35, and history of hypertension.

AF indicates atrial fibrillation; CAD, coronary artery disease; HF, heart failure; INR, international normalized ratio; LV, left ventricular; and TEE, transesophageal echo.

a. Anticoagulate patients in whom no thrombus is identified with intravenous unfractionated heparin by an initial bolus injection before cardioversion, followed by a continuous infusion in a dose adjusted to prolong the activated partial thromboplastin time at 1.5 to 2 times the reference control value. (*Level of Evidence: B*)

b. Next, provide oral anticoagulation (INR 2 to 3) for a period of at least 3 to 4 weeks, as for patients undergoing elective cardioversion. (*Level of Evidence: B*)

c. Limited data are available to support the subcutaneous administration of low-molecular-weight heparin in this indication. (*Level of Evidence: C*)

d. Treat patients in whom thrombus is identified by TEE with oral anticoagulation (INR 2 to 3) for at least 3 to 4 weeks before and after restoration of sinus rhythm. (*Level of Evidence: B*)

Class IIb

1. Cardioversion without TEE guidance during the first 48 h after the onset of AF. (*Level of Evidence: C*)

a. In these cases, anticoagulation before and after cardioversion is optional, depending on assessment of risk. (*Level of Evidence: C*)

2. Anticoagulate patients with atrial flutter undergoing cardioversion in the same way as for patients with AF. (*Level of Evidence: C*)

Recommendations for Prevention and Management of Postoperative AF

Class I

1. Treat patients undergoing cardiac surgery with an oral beta-blocker to prevent postoperative AF, unless contraindicated. (*Level of Evidence: A*)

2. In patients who develop postoperative AF, achieve rate control by administration of AV nodal blocking agents. (*Level of Evidence: B*)

Class IIa

1. Administer sotalol or amiodarone prophylactically to patients at increased risk of developing postoperative AF. (*Level of Evidence: B*)

2. Restore sinus rhythm in patients who develop postoperative AF by pharmacological cardioversion with ibutilide or direct-current cardioversion, as recommended for nonsurgical patients. (*Level of Evidence: B*)

3. In patients with recurrent or refractory postoperative AF, attempt maintenance of sinus rhythm by administration of antiarrhythmic medications, as recommended for patients with CAD who develop AF. (*Level of Evidence: B*)

4. Administer antithrombotic medication in patients who develop postoperative AF, as recommended for nonsurgical patients. (*Level of Evidence: B*)

Recommendations for Management of Patients With AF and Acute Myocardial Infarction

Class I

1. **Electrical cardioversion for patients with severe hemodynamic compromise or intractable ischemia. (*Level of Evidence: C*)**
2. **Intravenous administration of digitalis or amiodarone to slow a rapid ventricular response and improve LV function. (*Level of Evidence: C*)**
3. **Intravenous beta-blockers to slow a rapid ventricular response in patients without clinical LV dysfunction, bronchospastic disease, or AV block. (*Level of Evidence: C*)**
4. **Heparin for patients with AF and acute MI, unless contraindications to anticoagulation are present. (*Level of Evidence: C*)**

Class III

1. **Administer type IC antiarrhythmic drugs in patients with AF in the setting of acute myocardial infarction. (*Level of Evidence: C*)**

Recommendations for Management of AF and Ventricular Preexcitation

Class I

1. **Catheter ablation of the accessory pathway in symptomatic patients with AF who have WPW syndrome, particularly those with syncope due to rapid heart rate or those with a short bypass tract refractory period. (*Level of Evidence: B*)**
2. **Immediate electrical cardioversion to prevent ventricular fibrillation in patients with WPW in whom AF occurs with a rapid ventricular response associated with hemodynamic instability. (*Level of Evidence: B*)**
3. **Intravenous procainamide or ibutilide in an attempt to restore sinus rhythm in patients with WPW in whom AF occurs without hemodynamic instability in association with a wide QRS complex on the ECG (greater than or equal to 120 ms in duration). (*Level of Evidence: C*)**

Class IIb

1. **Administer intravenous quinidine, procainamide, disopyramide, ibutilide, or amiodarone to hemodynamically stable patients with AF involving conduction over an accessory pathway. (*Level of Evidence: B*)**
   a. **Immediate cardioversion is required when very rapid tachycardias or hemodynamic instability occurs in patients with AF involving conduction over an accessory pathway. (*Level of Evidence: B*)**

Class III

Intravenous administration of beta-blocking agents, digitalis glycosides, diltiazem, or verapamil in patients with WPW syndrome who have preexcited ventricular activation in AF. (*Level of Evidence: B*)

Recommendations for Management of AF in Patients With Hyperthyroidism

Class I

1. **Administer a beta-blocker as necessary to control the rate of ventricular response in patients with AF complicating thyrotoxicosis, unless contraindicated. (*Level of Evidence: B*)**
2. **In circumstances when a beta-blocker cannot be used, administer a calcium channel antagonist (diltiazem or verapamil) to control the ventricular rate. (*Level of Evidence: B*)**
3. **In patients with AF associated with thyrotoxicosis, use oral anticoagulation (INR 2 to 3) to prevent thromboembolism, as recommended for AF patients with other risk factors for stroke. (*Level of Evidence: C*)**
   a. **Once a euthyroid state is restored, recommendations for antithrombotic prophylaxis are the same as for patients without hyperthyroidism. (*Level of Evidence: C*)**

Recommendations for Management of AF During Pregnancy

Class I

1. **Control the rate of ventricular response with digoxin, a beta-blocker, or a calcium channel antagonist. (*Level of Evidence: C*)**
2. **Electrical cardioversion in patients who become hemodynamically unstable due to the dysrhythmia. (*Level of Evidence: C*)**
3. **Administer antithrombotic therapy (anticoagulant or aspirin) throughout pregnancy to all patients with AF (except those with lone AF). (*Level of Evidence: C*)**

Class IIb

1. **Attempt pharmacological cardioversion by administration of quinidine, procainamide, or sotalol in hemodynamically stable patients who develop AF during pregnancy. (*Level of Evidence: C*)**
2. **Administer heparin to patients with risk factors for thromboembolism during the first trimester and last month of pregnancy. Unfractionated heparin may be administered either by continuous intravenous infusion in a dose sufficient to prolong the activated partial thromboplastin time to 1.5 to 2 times the control (reference) value or by intermittent subcutaneous injection in a dose of 10,000 to 20,000 U every 12 h, adjusted to prolong the mid-interval (6 h after injection) activated partial thromboplastin time to 1.5 times control. (*Level of Evidence: B*)**
   a. **Limited data are available to support the subcutaneous administration of low-molecular-weight heparin for this indication. (*Level of Evidence: C*)**
3. **Administer an oral anticoagulant during the second trimester to patients at high thromboembolic risk. (*Level of Evidence: C*)**

Recommendations for Management of AF in Patients With HCM

Class I

Treat patients with HCM who develop AF with oral anticoagulation (INR 2 to 3), as recommended for other high-risk patients for prevention of thromboembolism. (*Level of Evidence: B*)

Class IIa

Antiarrhythmic medications to prevent recurrences. Available data are insufficient to recommend one agent over another in this situation, but disopyramide and amiodarone are generally preferred. (*Level of Evidence: C*)

Recommendations for Management of AF in Patients With Pulmonary Diseases

Class I

1. **In patients who develop AF during an acute pulmonary illness or exacerbation of chronic pulmonary disease, correction of hypoxemia and acidosis are the primary therapeutic measures. (*Level of Evidence: C*)**
2. **In patients with obstructive pulmonary disease who develop AF, a calcium channel antagonist agent (diltiazem or verapamil) is preferred for ventricular rate control. (*Level of Evidence: C*)**
3. **Attempt electrical cardioversion in patients with pulmonary disease who become hemodynamically unstable due to AF. (*Level of Evidence: C*)**

Class III

1. **Use of theophylline and beta-adrenergic agonist agents in patients with bronchospastic lung disease who develop AF. (*Level of Evidence: C*)**
2. **Use of beta-blockers, sotalol, propafenone, and adenosine in patients with obstructive lung disease who develop AF. (*Level of Evidence: C*)**

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