Contemporary Management of Atrial Fibrillation: Update on Anticoagulation and Invasive Management Strategies

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On completion of this article, you should be able to (1) assess patients with their first onset of atrial fibrillation and manage recurrent episodes, (2) place patients in categories on the basis of their risk of stroke and define the best anticoagulation management option for each patient, and (3) determine which patients may benefit from an invasive ablation-based approach for the management of atrial fibrillation.

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. Its increasing prevalence, particularly among the elderly, renders it one of the most serious current medical epidemics. Several management questions confront the clinician treating a patient with AF: Should the condition be treated? Is the patient at risk of death or serious morbidity as a result of this diagnosis? If treatment is necessary, is rate control or rhythm control superior? Which patients need anticoagulation therapy, and for how long? This review of articles obtained by a search of the PubMed and MEDLINE databases presents the available evidence that can guide the clinician in answering these questions. After discussing the merits of available therapy, including medications aimed at controlling rate, rhythm, or both, we focus on the present status of ablative therapy for AF. Catheter ablation, particularly targeting the pulmonary veins, is being increasingly performed, although the precise indications for this approach and its effectiveness and safety are being actively investigated. We briefly discuss other invasive options that are less frequently used, such as pacemakers, defibrillators, left atrial appendage closure devices, and the surgical maze procedure.

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AAD = antiarrhythmic drug; AF = atrial fibrillation; AFFIRM = Atrial Fibrillation Follow-up Investigation of Rhythm Management; CAST = Cardiac Arrhythmia Suppression Trial; CI = confidence interval; INR = international normalized ratio; OR = odds ratio; TIA = transient ischemic attack

Atrial fibrillation (AF) is the most common arrhythmia seen in clinical practice. This condition has been recognized as one of the most serious current medical epidemics. The prevalence of AF increases with the patient's age: it is found in 0.1% of adults younger than 55 years but in more than 9% of those aged 80 years or older. It is important to recognize that prevalence data are reported only for clinically recognized, symptomatic AF. The actual occurrence of asymptomatic AF is probably considerably higher.[1] It is estimated that 2.3 million adults in the United States have clinically recognized AF and have sought medical attention for this condition. This number is expected to increase to approximately 6 million by 2050.[1] This increasing number brings with it an increasing need for clinicians to counsel patients with AF by addressing several important issues, including a determination of the patient's risk of thromboembolic stroke or death and an understanding of the risks and benefits of the available treatment approaches. This review of the medical literature related to AF (obtained by searching PubMed and MEDLINE) presents the available evidence as a guide to the clinician.

CLASSIFICATION

Atrial fibrillation has been classified in several ways. *Lone* AF typically affects patients younger than 60 years who have no evidence of structural heart disease. Patients with lone AF are at a lower risk of thromboembolism than other patients with AF. One study found that, after 30 years of follow-up, the all-cause mortality rates of patients with lone AF are similar to those of age- and sex-matched controls older than 30 years who do not have AF.[2]

Some classification systems distinguish between *primary* AF and *secondary* AF. Secondary AF has an acute and possibly reversible cause, such as hyperthyroidism or acute alcohol intoxication. It may also occur after cardiac surgery.

Perhaps the most clinically relevant classification distinguishes between *paroxysmal* AF and *nonparoxysmal* AF. In many ways, these conditions are separate entities with marked differences in etiology and management options. Patients with paroxysmal AF experience episodes that terminate spontaneously within 7 days and usually

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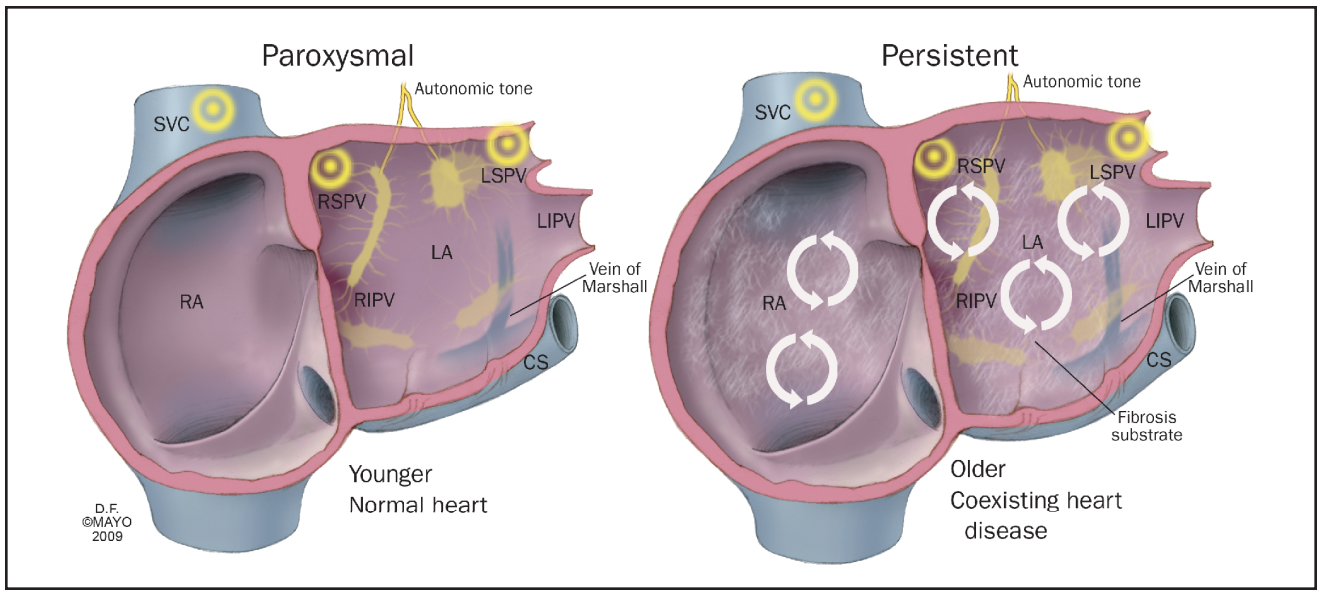


FIGURE 1. Important differences between the paroxysmal and persistent forms of atrial fibrillation. These differences have implications for management and for outcome expectations. Circular arrows represent rotors. CS = coronary sinus; LA = left atrium; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RA = right atrium; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein; SVC = superior vena cava.

within 24 hours.[3] Approximately 40% of all AF cases are paroxysmal. Nonparoxysmal AF is often further classified as *persistent* or *permanent*. Both terms describe episodes that last longer than 7 days and require cardioversion for termination. However, permanent AF refers to those cases in which AF has existed for many years and cannot be consistently terminated with cardioversion.[4-6]

Paroxysmal AF is typically a disease of the thoracic vein and the autonomic nervous system in which pathological triggers repeatedly reinitiate AF. Patients with paroxysmal AF are often younger than those with other types of AF and have no structural heart disease (Figure 1). Persistent AF and permanent AF are primarily diseases of abnormal atrial substrate. They are often characterized histopathologically by marked atrial enlargement with fibrosis and electrophysiologically by multiple reentrant circuits with even minor triggers that can reinitiate and maintain AF.

Nonparoxysmal AF is characterized by abnormal triggers that are often extra-atrial and by abnormal atrial myocardium, often resulting in wide variations in treatment approaches (see Pathophysiology and Disease Association). In as many as 25% of patients, paroxysmal AF will progress to chronic or permanent AF within 5 years.[4,5]

PATHOPHYSIOLOGY AND DISEASE ASSOCIATION

The exact cause of AF is unknown. A complex interplay exists between triggers that initiate AF and abnormalities in the atrial myocardial substrate that allow perpetuation of the arrhythmia. Although investigators and clinicians have debated for decades whether triggers or substrates (automatic foci or multiple reentrant wavelets) are primarily responsible for AF, newer insights suggest that both mechanisms may be operative for most patients. Recently, 2 important concepts have been elucidated. First, the more frequently AF occurs, the greater the likelihood of a further increase in the frequency and duration of episodes (AF begets AF).[7] Second, most triggers that initiate AF appear to arise not from the atria but rather from some anatomic neighbor of the atria, such as a pulmonary vein, the superior vena cava, or the retro-atrial ganglionated plexuses.[8]

Comorbid Conditions

Of the comorbid conditions associated with AF, hypertension is the most common. Diastolic dysfunction of the ventricles does not allow their normal atrial filling. The resultant back-pressure causes hypertrophy of cardiac myocytes, proliferation of fibrous tissue, and decreases in intercellular coupling.[9] Aggressive management of hypertension may also result in clinical improvement of AF.[10]

Atrial fibrillation is common among patients with coronary artery disease. However, ischemia of the atrium rarely causes AF. Patients with coronary artery disease often exhibit hypertension and left ventricular dysfunction with secondary abnormalities in the atrium.[11] Atrial fibrillation also occurs in approximately 8.6% of patients with acute

coronary syndromes, but again the phenomenon is probably secondary and is not a direct correlate of ischemia.[12]

Obesity is another important risk factor for AF. A recent meta-analysis found that obesity increases the risk of AF by 49% in the general population and that the risk escalates in parallel with the body mass index.[13] The association between AF and sleep apnea with or without coexisting obesity is also well recognized. Ongoing studies are attempting to discern whether sleep apnea is a causative factor for AF and whether aggressive management of sleep apnea could affect the occurrence of symptomatic AF episodes.[14]

Overt hyperthyroidism is a well-known cause of AF. Findings show that even subclinical hyperthyroidism may be a risk factor for AF.[15,16] A study involving a group of elderly patients with normal thyroid-stimulating hormone levels found that an elevation in the concentration of free thyroxine was independently associated with AF.[16]

Structural heart disease is strongly associated with AF.[17,18] Valvular heart disease has long been recognized as a risk factor for AF. One study found that the prevalence of AF in combination with rheumatic valvular disease varies from 16% (in association with isolated mitral regurgitation) to 70% (in association with mitral stenosis and other valvular disease).[19] In patients with degenerative mitral valve regurgitation, AF is a marker of disease progression and is an independent factor that should be considered in the timing of mitral valve surgery.[20,21] The existence of AF before mitral valve surgery (particularly mitral valve repair) negatively affects early and late survival rates.[22] Approximately 5% of patients with aortic stenosis have poorly tolerated AF, and this condition may be the first sign of clinical decompensation that brings the diagnosis to light.[23] Approximately 20% to 25% of patients with hypertrophic cardiomyopathy have AF, which is associated with an increased risk of death due to heart failure.[24,25]

Postoperative AF

Atrial fibrillation is common after cardiac surgery: postoperative AF occurs in as many as 40% of patients undergoing coronary artery bypass grafting or valve surgery and in as many as 60% of those undergoing combined bypass and valve surgery.[25-27] Although the exact causes of postoperative AF are unknown, pericarditis, changes in autonomic tone, and large shifts in fluid volume are thought to contribute to its incidence. Preoperative prophylaxis with β-blockers, amiodarone, corticosteroids, and, more recently, lipid-lowering agents has generally reduced the incidence of postoperative AF.[28-31]

Autonomic Dysfunction

Intense study is currently being devoted to defining the role of the autonomic nervous system in causing AF. The vagal innervation of the atria is widespread and asymmetrical, and vagal stimulation shortens the refractory period to various extents in different parts of the atrium, thereby increasing the likelihood of AF.[32,33] In certain patients, increased sympathetic tone brings on episodes of AF, and it is likely that sympathovagal balance also plays a role in initiating AF.[34-36]

Alcohol and Caffeine

Binge drinking of alcohol has been associated with AF, producing what is called the *holiday heart syndrome*. Observational studies have also found an association between sustained heavy use of alcohol and AF.[3,37,38] Although patients are typically advised to moderate their caffeine intake, no association between caffeine and AF has yet been found. One observational study involving 47,949 patients found no association between caffeine consumption and AF or flutter.[39]

Inflammation

Inflammation may play an important role in both triggering and maintaining AF.[40] Several studies have documented the association between elevated C-reactive protein concentrations and AF. In addition, left atrial dysfunction may occur with increased C-reactive protein concentrations even without AF.[41-43] These findings imply that inflammation alone may affect left atrial function and give rise to electrical derangement.[44]

Renin-Angiotensin System

Recent findings suggest that the renin-angiotensin system plays an active role in the generation and maintenance of AF.[45] Angiotensin II is a potent atrial fibrotic agent that secondarily increases intra-atrial pressures, thereby contributing to atrial stretch.[46] An accumulating body of evidence shows that inhibiting the renin-angiotensin system protects atrial remodeling and promotes the maintenance of sinus rhythm.[47,48]

Genetic Factors

Framingham data show that 30% of patients with AF have a family history of AF.[49] Most AF is probably due to polygenic inheritance or a combined effect of the number of genes. The first loci of familial AF was identified on chromosome 10q22-24 in 1997; since then, several loci have been mapped.[50] Genes implicated in monogenic inheritance have been recently identified, including the *KCNQ1* and *SCN5A* genes.[51]

Summary

Atrial fibrillation is best considered to be a symptom of a more widespread process. Common associations include diastolic ventricular dysfunction and aging. Whether aging alone or inflammation and autonomic imbalance are the primary "causes" of AF is currently under investigation.

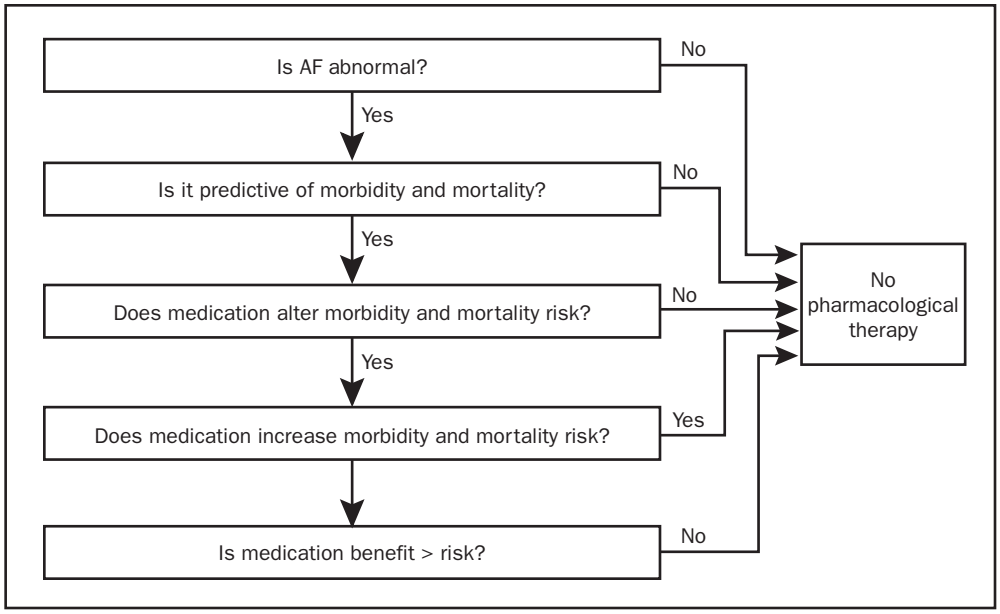


FIGURE 2. Criteria for treating atrial fibrillation (AF). The primary criterion for treating AF is symptom relief. Currently, no conclusive evidence suggests that maintaining sinus rhythm decreases the rates of mortality or severe morbidity. This absence of evidence is probably due to the fact that minimal or no risk of mortality is associated with AF alone, that previously studied methods of maintaining sinus rhythm have been ineffective, and that both pharmacological therapy and invasive therapy are themselves associated with particular risks.

DIAGNOSIS

Clinical Manifestation

The diagnosis of AF is generally straightforward. Typical symptoms include irregular palpitation of sudden onset, associated with fatigue. The clinical spectrum, however, is highly variable: some patients experience severe discomfort from palpitations, whereas others have absolutely no symptoms and AF is an incidental diagnosis.[52] More difficult to evaluate are cases of chronic AF in which patients perceive no palpitation but report either episodic or worsening weakness, shortness of breath, or fatigue. It is difficult to assign a cause even to episodic AF in a patient with nonspecific symptoms because more than 17% of patients undergoing random continuous monitoring exhibit episodes of AF.[53]

Electrocardiography and Monitoring

Electrocardiography is the mainstay for diagnosing AF. Characteristic irregular fibrillatory waves at 350 to 600 pulses/min in the atrium in conjunction with irregular QRS complexes (90 to 170 beats/min) are diagnostic.[54] Atrial flutter, which produces more regular sawtooth-type flutter waves, may paradoxically be associated with higher ventricular rates.

For the diagnosis of paroxysmal AF, some form of long-term monitoring is needed. In patients with relatively frequent or daily episodes, a 24- to 48-hour Holter monitor is sufficient. When palpitations or unexplained symptoms occur only rarely, 30-day event monitors or implantable recording devices can be used.[55]

WHY TREAT AF?

When counseling patients with AF, clinicians should consider such crucial questions as whether AF can be life threatening and what the long-term consequences of untreated AF may be (Figure 2). The longer AF is allowed to exist, the easier it becomes to reinduce and to sustain this arrhythmia. This concept that "AF begets AF" was first demonstrated in 1995 by an important and illustrative mechanistic study using animals.[7]

AF and Total Mortality

Despite the abundance of studies, a crucial but difficult question is whether AF is an independent risk factor for mortality in all patients. In the Framingham cohort, the odds ratio (OR) for total mortality (number of deaths per 100,000 population) was 1.5 for men and 1.9 for women with AF, even after the analysis was adjusted for age, overt heart disease, and other risk factors.[56]

Importantly, no current findings suggest that treating the arrhythmia contributes to a reduction in any potentially enhanced mortality rate. Therefore, patients cannot be

counseled to undergo any form of rhythm control with the expectation of improving their chances of survival. The reasons for the absence of such findings may be that mortality rates associated with AF are not enhanced to begin with or that the proarrhythmic potential of antiarrhythmic agents is offset by the procedural risks associated with invasive therapies.

Thromboembolism and Stroke

Thromboembolic stroke may be associated with AF. The overall risk of thromboembolism is approximately 5% per year, although the risk associated with individual risk factors varies widely.[57,58] The exact cause of the association between AF and thromboembolism is unknown and may in part be an epiphenomenon: that is, although most emboli probably originate from the left atrium, as many as one-fourth or more may not, such as embolism resulting from the carotid arteries.

Tachycardia-Mediated Cardiomyopathy

A small subset of patients with AF experience dilated cardiomyopathy (tachycardia-mediated cardiomyopathy). Typically, patients have rapid ventricular rates and relatively persistent AF. The prevalence has not been clearly determined, but a study involving a series of 673 patients with dilated cardiomyopathy found that only 1 case of AF was caused by tachycardia.[59] Atrial fibrillation may not only cause the cardiomyopathy but may also exacerbate the symptoms of heart failure as a result of diastolic filling abnormalities and tachycardia-induced systolic dysfunction. Various cellular mechanisms have been implicated as causes of tachycardia-mediated cardiomyopathy, including the depletion of myocardial energy stores by chronic tachycardia, which causes oxidative stress and injury and leads to abnormal calcium handling and β-adrenergic responsiveness.[54]

Quality of Life

The primary reason for treating AF is to improve the patient's quality of life by decreasing the frequency and severity of AF-related symptoms. It has been documented that the quality of life of patients with AF is poor in comparison with that of healthy controls, the general population, and other patients with coronary artery disease.[60] Both rate control and rhythm control improve quality of life, and most studies show that controlling both produces a somewhat greater benefit than controlling rate alone. However, the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial found no difference in patients' quality of life, regardless of whether a rate or rhythm control strategy was used.[61]

It should be noted that younger patients, particularly those with paroxysmal AF and rapid ventricular rates, may exhibit symptoms that are difficult to manage with rate control approaches alone.

MANAGEMENT OF NEW-ONSET AF

Hemodynamic stability must first be assessed. A hemodynamically unstable patient should undergo emergency direct current cardioversion.[62] Most patients, however, are relatively stable hemodynamically, and the goal of therapy for them is ventricular rate control with a target heart rate lower than 100 beats/min. Either oral or intravenous atrioventricular nodal blocking agents are used. Calcium channel blockers or β-blockers are the first-line agents, and digoxin is sometimes added. Diltiazem is generally preferable to verapamil because it is associated with fewer negative inotropic effects and less peripheral vasodilation. β-Blockers are more effective for patients with higher adrenergic tones, such as those with postoperative AF.

Some patients with infrequent but highly symptomatic acute episodes of AF can be managed without regular dosing of flecainide or propafenone. This so-called pill-in-the pocket[63] is taken by the patient at the first sign of AF. This therapy should be initiated in a monitored setting so that the risk of proarrhythmia can be assessed.

For patients with acute AF that is sustained and continues to be symptomatic despite attempts at rate control, electrical or pharmacological cardioversion should be considered.[64]

Direct Current Cardioversion

Approximately one-half to two-thirds of patients with acute-onset AF will experience spontaneous conversion to sinus rhythm within 24 hours. If spontaneous conversion to a normal rhythm does not occur within this time period and the AF continues to cause symptoms, cardioversion should be considered. Electrical cardioversion is highly effective (90%) but requires sedation or general anesthesia. If the episode of AF is known to have persisted for less than 48 hours, the risk of stroke after cardioversion is low.[65] In these cases, cardioversion can be performed without transesophageal echocardiography or oral anticoagulation. For cases in which the AF lasts longer, the risk of stroke after cardioversion is high (6%-7%), although adequate anticoagulation decreases this risk to less than 1%.[65] Although direct current cardioversion with biphasic wave forms is highly effective in the conversion of AF, the AF commonly recurs. Patients should be told that cardioversion itself is not a treatment for AF and that recurrence should be expected at some point.

TABLE 1. **Risk of Stroke According to $CHADS_2$ Score as Determined by Data From NRAF[a]**

$CHADS_2$ score	No. of patients (N=1733)	No. of strokes (n=94)	NRAF crude stroke rate per 100 patient-years, %	NRAF adjusted stroke rate, % (95% CI)[b]
0	120	2	1.2	1.9 (1.2-3.0)
1	463	17	2.8	2.8 (2.0-3.8)
2	523	23	3.6	4.0 (3.1-5.1)
3	337	25	6.4	5.9 (4.6-7.3)
4	220	19	8.0	8.5 (6.3-11.1)
5	65	6	7.7	12.5 (8.2-17.5)
6	5	2	44.0	18.2 (10.5-27.4)

[a] $CHADS_2$ = *c*ardiac failure (recent congestive heart failure, 1 point), history of *h*ypertension (1 point), *a*ge 75 years or older (1 point), *d*iabetes mellitus (1 point), and history of *s*troke or transient ischemic attack (2 points); CI = confidence interval; NRAF = National Registry of Atrial Fibrillation.

[b] The adjusted stroke rate is the expected stroke rate per 100 patient-years from the exponential survival model, assuming that aspirin was not taken.

Data from *JAMA*.[80]

Pharmacological Cardioversion

Pharmacological cardioversion has the advantage of avoiding anesthesia but is less effective than electrical cardioversion.[66] If administered within 24 hours of onset, class I or III antiarrhythmic drugs (AADs) can achieve cardioversion for 47% to 84% of patients. When the AF has persisted for more than 48 hours, drugs are effective for only 15% to 30% of patients.[3]

LONG-TERM MANAGEMENT OF AF

Although this review briefly discusses the choice of rate control or rhythm control and the guidelines for the use of antiarrhythmic agents, it focuses primarily on the crucial issue of stroke prevention and the increasingly important role of radiofrequency ablation.

Preventing Stroke in Patients With AF

Preventing thromboembolic complications, especially stroke, is a primary goal of AF treatment. Atrial fibrillation is associated with a nearly 5-fold increase in the risk of stroke.[67,68] The Framingham study found that the age-adjusted 2-year incidence of symptomatic stroke was 4.8% among patients with AF and 1% among patients without AF.[67] For octogenarians, nearly one-fourth of all strokes are attributable to AF.[67] Strokes tend to be more severe and disabling for patients with AF than for those without AF.[69,70]

Mechanisms of Stroke. Multiple pathophysiologic mechanisms contribute to the link between AF and stroke. Atrial fibrillation impairs atrial contraction, and this impairment in turn promotes blood stasis in the left atrium.[71] In addition, AF is associated with a hypercoagulable state in which the plasma concentration of fibrinopeptide A is elevated and that of antithrombin III is decreased.[72,73] Taken together, stasis and hypercoagulability can lead to atrial thrombus formation, particularly in the left atrial appendage.[74] Left atrial thrombus can then break free of the left atrium and embolize to the brain, thereby resulting in an ischemic stroke. The presence of a thrombus in the left atrial appendage is associated with a 3-fold increase in the risk of stroke.[74]

Determining the Clinical Risk of Stroke. The risk of stroke varies widely among patients with AF, depending on the presence or absence of several risk factors.[57,75-83] Risk factors that put AF patients at high risk of future stroke include rheumatic mitral valve disease, the presence of a mechanical heart valve, and prior thromboembolism.[78,80] Among patients with so-called nonvalvular AF (no rheumatic mitral valve disease and no mechanical heart valve), the risk factors for stroke can be conveniently remembered by using the mnemonic $CHADS_2$, which stands for *c*ardiac failure (recent congestive heart failure), history of *h*ypertension, *a*ge 75 years or older, *d*iabetes mellitus, and history of *s*troke or transient ischemic attack (TIA)[80] (Table 1).

$CHADS_2$ also refers to a scoring system designed to estimate the risk of stroke among patients with AF.[80] The $CHADS_2$ scoring system was derived from a study involving 1733 Medicare beneficiaries and was subsequently validated by a larger study involving 11,526 patients enrolled in an integrated health care system.[80,81] The $CHADS_2$ score system provides an estimate of a patient's risk of stroke. The system assigns 1 point each for cardiac failure (recent congestive heart failure), history of hypertension, age 75 years or older, and diabetes and assigns 2 points for a history of stroke or TIA (thus the inclusion of the number 2 in the mnemonic). The sum of the points determines the $CHADS_2$ score. The adjusted annual stroke rate increases from 1.9% for patients with a $CHADS_2$ score of 0 to 18.2% for patients with a $CHADS_2$ score of 6.

Pharmacological Prevention of Stroke. Several randomized trials have assessed the ability of warfarin or aspirin to reduce the risk of AF-associated stroke.[84-91] Hart et al[82] pooled the data from these trials to compare the

effectiveness of adjusted-dose warfarin vs placebo, aspirin vs placebo, and adjusted-dose warfarin vs aspirin for the prevention of stroke among patients with AF. This meta-analysis showed that adjusted-dose warfarin is remarkably effective in reducing the risk of stroke for patients with AF.[92] Compared with placebo, adjusted-dose warfarin decreased the relative risk of stroke by 62% (95% confidence interval [CI], 48%-72%).[82] The absolute reduction of stroke risk by adjusted-dose warfarin vs placebo was 2.7% annually for primary prevention and 8.4% annually for secondary prevention. The rate of cerebral hemorrhage was 0.3% per year for patients receiving adjusted-dose warfarin and 0.1% per year for patients receiving placebo. Adjusted-dose warfarin also decreased all-cause mortality rates by 26% (95% CI, 4%-43%) in relative terms and by 1.6% in absolute terms.

Aspirin is generally less effective than warfarin in reducing the risk of AF-associated stroke.[82] An analysis of pooled data from randomized trials comparing antiplatelet therapy (mainly aspirin) and placebo for the prophylaxis of AF-associated stroke showed that aspirin was associated with a relative reduction of the risk of stroke of 22% (95% CI, 2%-38%).[82] The absolute reduction of stroke risk by aspirin vs placebo was 1.5% annually for primary prevention and 2.5% annually for secondary prevention. Aspirin use was not associated with a statistically significant reduction in all-cause mortality. The direct comparison of adjusted-dose warfarin and aspirin showed that adjusted-dose warfarin decreased the relative risk of stroke by 36% (95% CI, 14%-52%).[82] The use of warfarin, however, was associated with a 2.1-fold higher relative risk of intracranial hemorrhage than the use of aspirin. This analysis found no statistically significant difference in survival rates between patients who received warfarin and those who received aspirin.

Which patients should receive aspirin and which should receive oral anticoagulation (warfarin) for long-term prophylaxis against AF-associated thromboembolism? The guidelines of the American College of Cardiology, the American Heart Association, and the European Society of Cardiology for administering antithrombotic therapy to patients with AF are summarized in Table 2.[3] In general, patients with no risk factors for stroke (a $CHADS_2$ score of 0)[80] should take 81 to 325 mg/d of aspirin. Patients with 1 moderate risk factor for stroke (a $CHADS_2$ score of 1) should take either 81 to 325 mg/d of aspirin or adjusted-dose warfarin with a target international normalized ratio (INR) of 2.5 (range, 2.0-3.0). Patients with risk factors that confer a high risk of stroke (a previous stroke or TIA, rheumatic mitral stenosis, or a $CHADS_2$ score of 2 or higher) should take adjusted-dose warfarin with a target INR of 2.5 (range, 2.0-3.0). Because patients with hypertrophic cardiomyopathy and AF have relatively high rates of thromboembolic complications, anticoagulation with adjusted-dose warfarin (target INR, 2.5; range, 2.0-3.0) should also be strongly considered for these patients.[3,25] The intensity of anticoagulation for patients with AF and a mechanical heart valve depends on the type of valve, but the target INR is usually at least 2.5.[3]

TABLE 2. **Antithrombotic Therapy for Patients With Atrial Fibrillation**[a]

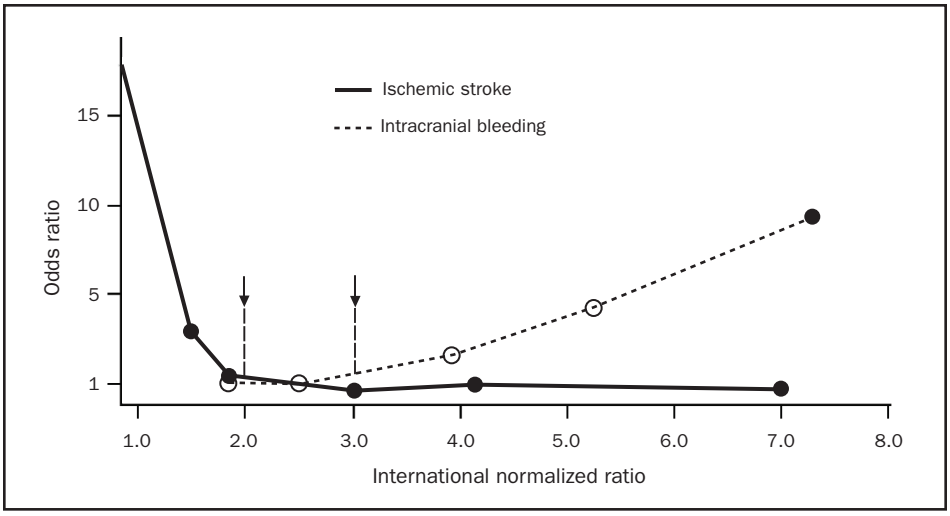
Risk category	Recommended therapy	
No risk factors	Aspirin, 81-325 mg/d	
One moderate-risk factor	Aspirin, 81-325 mg/d or warfarin (target INR, 2.5; range, 2.0-3.0)	
Any high-risk factor or more than 1 risk factor	Warfarin (target INR, 2.5; range, 2.0-3.0)	
Less validated or weaker risk factors	**Moderate-risk factors**	**High-risk factors**
Female sex	Age ≥75 y	Previous stroke, TIA, or embolism
Age, 65-74 y	Hypertension	Mitral stenosis
Coronary artery disease	Heart failure	Prosthetic heart valve[b]
Thyrotoxicosis	LVEF ≤35%	
	Diabetes mellitus	

[a] INR = international normalized ratio; LVEF = left ventricular ejection fraction; TIA = transient ischemic attack.
[b] If the patient has a mechanical valve, the target INR should be higher than 2.5.

Goal INR. Maintaining INR[84] levels within a range of 2.0 to 3.0 minimizes the incidence of both ischemic and hemorrhagic stroke[3,93,94] (Figure 3). The crucial relationship between low INR levels (below 2.0) and an increased risk of ischemic stroke was confirmed by the results of the AFFIRM trial: 72% of the 157 patients who experienced ischemic strokes during the trial had INR levels below 2.0 near the time of the strokes.[96] For patients with contraindications to warfarin therapy, 81 to 325 mg/d of aspirin should be considered for the prophylaxis of thromboembolism.[3] A target INR of 3.0 (range, 2.5-3.5) may be appropriate for patients at very high risk of thromboembolism or for those who experience thromboembolism even with an INR of 2.0 to 3.0.[3]

Antithrombotic Therapy: Clinical Pearls and Special Circumstances. Several facts about long-term antithrombotic therapy for patients with AF should be kept in mind. First, atrial flutter should be treated in the same manner as AF with regard to antithrombotic therapy.[3] This recommendation is based on the recognition that the stroke risks associated with atrial flutter and AF are comparable and that AF commonly develops in patients with atrial flutter.[97,98]

Second, the pattern of AF (paroxysmal, persistent, or permanent) generally does not influence the method or degree of antithrombotic treatment for AF.[3] The Stroke Prevention in Atrial Fibrillation study found that the annual stroke rate for patients with intermittent AF (3.2%) was very similar to that for patients with sustained AF (3.3%).[6]



FIGUR E 3. Odds ratios for stroke and intracranial bleeding according to the international normalized ratio (INR) for patients with atrial fibrillation. The risk of ischemic stroke is higher for patients with an INR lower than 2, and the risk of intracranial bleeding is higher when the INR is higher than 3 (arrows). Adapted from *Ann Intern Med*,[95] with permission.

Third, AADs do not reduce the need for long-term antithrombotic therapy aimed at preventing stroke. The AFFIRM trial found no statistically significant difference in stroke rate between patients treated with rate control (who were predominantly in AF) and those treated with AADs (who were predominantly in sinus rhythm).[96] Most of the ischemic strokes in the rhythm control arm of AFFIRM occurred after warfarin was discontinued.[96] Strokes are not unexpected among patients with seemingly successful restoration of sinus rhythm given the fact that asymptomatic AF is common.[99,100]

Fourth, although left atrial ablation may eliminate symptomatic AF, long-term antithrombotic therapy should still be strongly considered after ablation. An observational study of postablation thromboembolic events raised the possibility that patients with risk factors for stroke may be able to forgo long-term anticoagulation after ablation.[101] Nonetheless, asymptomatic AF has been documented in patients who have undergone apparently successful left atrial ablation.[99] As a result, we generally base our recommendations regarding the need for postablation long-term antithrombotic therapy on well-validated risk stratification methods such as $CHADS_2$.[81]

Fifth, the combination of aspirin and clopidogrel should not be considered an adequate substitute for warfarin-based anticoagulation for patients with AF. The risk of stroke is 1.72-fold higher for patients taking aspirin plus clopidogrel than for those taking adjusted-dose warfarin.[102]

Sixth, the addition of antiplatelet therapy to adjusted-dose warfarin for patients with AF should be approached cautiously. Using aspirin in addition to warfarin has been found to increase elderly patients' absolute risk of serious bleeding by 0.6% during a 90-day observation period and to increase their relative risk of intracranial hemorrhage by a factor of 2.4.[92,103] For patients with chronic stable coronary artery disease and AF, adjusted-dose warfarin without aspirin is probably sufficient.[3,104] Observational data suggest that the combination of aspirin, clopidogrel, and warfarin may be associated with a high risk of bleeding.[105,106] Antithrombotic therapy for patients with a drug-eluting coronary stent and AF should be individualized, with consideration given to the use of adjusted-dose warfarin plus clopidogrel without aspirin.[3,106]

Anticoagulation and Cardioversion. The risk of thromboembolism is elevated during the first several days after cardioversion from atrial flutter or AF to sinus rhythm. Cardioversion resulting from electric shock, AAD therapy, pacing, or ablation, as well as spontaneous cardioversion, can result in transient atrial stunning or loss of atrial contraction.[107-109] This stunning after cardioversion may persist for days or weeks.[110,111] Stunning may promote atrial blood stasis and thrombus formation, which, in turn, can lead to stroke.[112-114] Cardioversion may also cause a stroke by dislodging a preexisting thrombus in the left atrial appendage. Most strokes and other thromboembolic episodes after cardioversion occur within the first 10 days.[114] In the absence of anticoagulation, the rate of cardioversion-associated thromboembolism may exceed 5%.[115] Anticoagulation decreases the rate of cardioversion-associated thromboembolism to less than 1%.[116,117] As a result, patients with AF that has persisted for more than 48 hours or for an unknown

duration should receive anticoagulation therapy (goal INR, 2.0-3.0) for 3 weeks before and 4 weeks after cardioversion.[3] Alternatively, anticoagulation with heparin (to an activated partial thromboplastin time 1.5 to 2 times higher than normal) can be initiated at the time of transesophageal echocardiography; if no intracardiac thrombus is identified, cardioversion can be performed with heparin bridging[118,119] until an INR of 2.0 has been obtained. At that point, heparin should be discontinued and warfarin therapy should be continued for 4 weeks with a target INR of 2.5 (range, 2.0-3.0).[3,118-120] If transesophageal echocardiography shows atrial thrombus, patients should undergo anticoagulation with heparin bridging[118,119] to warfarin therapy for 4 weeks with a target INR of 2.0 to 3.0 before cardioversion is attempted.

In general, patients with atrial flutter should undergo treatment similar to that for patients with AF with regard to anticoagulation near the time of cardioversion.[3,121]

For every patient with AF, the thromboembolic risk should be assessed by the $CHADS_2$ score, and the appropriate antithrombotic approach should be initiated. Importantly, the coexisting risk factors are at least as important as the presence of AF itself in defining stroke risk. Furthermore, rhythm control strategies should be undertaken for symptom management with the understanding that they will have no effect on the risk of stroke.

Rate Control or Rhythm Control for Symptom Management

Historically, it was assumed that maintaining sinus rhythm was better than controlling ventricular rates. This assumption was based on the theory that this practice would lead to more normal hemodynamics and a lower risk of thromboembolism. The landmark AFFIRM study and other key trials have definitively shown that, particularly among older patients, outcomes are not significantly different when rhythm vs rate is controlled.[96] We examined mortality data from 6 recent clinical trials involving 3303 patients assigned to rate control and 3312 patients assigned to rhythm control; this analysis included data from the 2007 AF-CHF (Atrial Fibrillation and Congestive Heart Failure) trial.[96,122-125] A comparison of the 2 groups demonstrated a relative risk of mortality of 0.95 (95% CI, 0.86-1.05) for the patients assigned to rate control (Figure 4).

Subset analysis of the data from the AFFIRM trial has shown that rhythm control yields some benefit for younger patients with symptomatic AF. Although the decision to initiate rhythm control must be individualized for each patient, younger patients with severe symptoms and comorbid conditions generally appear to benefit more from rhythm control than from rate control alone.

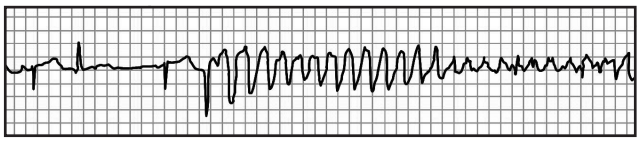


FIGURE 4. Most antiarrhythmic medications have a proarrhythmic potential. Pictured here is the proarrhythmia of concern when potassium channel blockers such as sotalol are used. Cause-dependent premature ventricular contractions triggering polymorphic ventricular tachycardia are seen.

Rate control should always be attempted first. Even when rhythm control is preferable, ventricular rates should be controlled because breakthrough AF should be expected. Generally, rate control is safe and effective and is sufficient for most patients. β-Blockers are the typical first-line agents, especially if other comorbid conditions (eg, coronary artery disease) necessitate their use. Calcium channel blockers and digoxin, as previously described, are also used in selected situations. If adequate rate control is obtained but symptoms persist, either from the arrhythmia itself or from the adverse effects of the rate-controlling medication, rhythm control should be attempted.

Pharmacological Therapy for Maintaining Sinus Rhythm

The primary goal of AAD therapy is to improve quality of life of patients with AF that remains symptomatic despite attempts at rate control (Table 3). Currently, the overall effectiveness of available AADs in maintaining long-term sinus rhythm is poor. The CACAF (Catheter Ablation for the Cure of Atrial Fibrillation) trial involved patients with paroxysmal or persistent AF for whom 2 previous AADs had failed. These patients were randomly assigned to catheter ablation or a control group. Of the 69 patients in the control group who had started AAD therapy, 63 (91.3%) experienced a recurrence of AF within 12 months.[126] The A4 (Catheter Ablation Versus Antiarrhythmic Drugs for Atrial Fibrillation) study[127] and the APAF (Ablation for Paroxysmal Atrial Fibrillation) trial also randomly assigned patients with AF for whom AAD therapy had failed to ablation or another AAD.[128] The results were similar to those of the CACAF trial: of the patients treated with AAD, 94% of those in the A4 study and 78% of those in the APAF trial experienced a recurrence of AF within 1 year. A recent systematic review analyzed data from 11,322 patients with AF enrolled in 44 clinical trials of AADs vs placebo or another AAD. The 1-year pooled AF recurrence rate was high: 71% to 84% for control patients and 44% to 67% for treated patients.[129] Amiodarone was the most effective agent for preventing recurrent AF (OR, 0.31 compared with all class I drugs; OR, 0.30 compared with sotalol).[129] No important differences in efficacy or safety were detected for the other antiarrhythmic agents studied.

TABLE 3. **Drug Approach to Patients With Atrial Fibrillation**

	Normal heart	Postmyocardial infarction/ ischemia	Hypertrophy/ hypertrophic myopathy	Dilated cardiomyopathy
Proarrhythmic risk	Low	High	Moderate	High
1st choice	Propafenone Flecainide	Dofetilide[a] Sotalol	Flecainide Propafenone	Amiodarone Dofetilide[a]
2nd choice	Sotalol Dofetilide[a] Disopyramide	Amiodarone Azimilide Dronedarone	Amiodarone Azimilide?	Azimilide? Quinidine Procainamide
Gray zone[b]	Quinidine Procainamide Amiodarone	Propafenone Quinidine	Dofetilide[a] Disophyramide	Quinidine Propafenone Sotalol
Do not use		Flecainide Encainide d-Sotalol	Quinidine	Flecainide Disopyramide

[a] Less useful in patients with paroxysmal atrial fibrillation.
[b] No clear or well-defined indication or contraindication.

In addition to their lack of effectiveness, antiarrhythmic medications may be associated with substantial toxicity. In a recent systematic review, 9% to 23% of patients taking AADs withdrew from clinical trials because of adverse effects.[129] Significantly fewer patients taking amiodarone withdrew from trials (OR, 0.52; *P*=.004), but this agent was associated with a number of toxic effects.

The primary determinant of the risk of proarrhythmia with AAD therapy is the presence of structural heart disease. Flecainide and propafenone can be used safely to treat patients with normal ventricular function and no coronary disease.[130] For those with systolic heart failure, amiodarone or dofetilide is preferred. The landmark Cardiac Arrhythmia Suppression Trial (CAST) showed that the mortality rate associated with flecainide administration was higher for patients with structural heart disease.[131] It should be noted that in this trial flecainide was used to suppress ventricular ectopy in patients with coronary artery disease. Nevertheless, on the basis of such findings, class IC agents are used for patients with no coexisting heart disease. Although amiodarone is associated with a lower risk of proarrhythmia than flecainide, its use is limited by serious extracardiac organ toxicity. Dofetilide can be administered to patients with systolic dysfunction, but its use requires inpatient observation, careful dose initiation and titration, and monitoring of the QT interval. Neither dofetilide nor sotalol can be administered to patients with serious renal dysfunction. For patients with left ventricular hypertrophy, dofetilide and sotalol are relatively contraindicated, and amiodarone is preferred. Dofetilide is less useful for patients with paroxysmal AF.

New antiarrhythmic agents are being actively investigated. Dronedarone is a noniodinated amiodarone derivative that produces similar cardiac effects but with less toxicity[132] because the iodine moiety of amiodarone is thought to be responsible for many of its adverse effects. Dronedarone has been shown to be more effective than placebo in preventing the recurrence of AF,[133] although the Antiarrhythmic Trial With Dronedarone in Moderate-to-Severe Congestive Heart Failure Evaluating Morbidity Decrease (ANDROMEDA) was stopped prematurely because of increased mortality rates among patients with heart failure who were assigned to the dronedarone arm. Tedisamil, another new AAD that was initially developed to treat ischemia by potassium channel blockade, is a class III antiarrhythmic agent that has been shown to be superior to placebo in converting AF to sinus rhythm. The drug may be proarrhythmic: 2 (1.8%) of 175 patients experienced self-terminating ventricular tachycardia.[134,135] Blockers of specific atrial channels, such as I_{KACh} and I_{Kur}, should produce no ventricular proarrhythmic adverse effects and are being actively investigated.[136,137]

Several nontraditional (not typically thought of as AADs) medications have been shown to be effective in preventing AF. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers have been found to prevent AF in patients with left ventricular hypertrophy or heart failure.[138] Lipid-lowering agents (statins) have also been shown to decrease the incidence of AF for patients with coronary artery disease and left ventricular dysfunction.[30] Fish oil may reduce the incidence of AF by altering the composition of the atrial myocyte membrane.[139] Another strategy targeting the inflammatory response that seems to be associated with AF is the administration of corticosteroids.[29,140]

Nonpharmacological Management of AF

Because of the limitations of pharmacological therapy in managing AF, several nonpharmacological approaches have been tried during the past 2 decades. These approaches

include pacemakers with specific algorithms and lead placement, atrial cardioverter-defibrillators, the surgical maze procedure, and radiofrequency ablation. Device (pacemaker and cardioverter-defibrillator) therapy for AF is infrequently used because of poor results in improving the symptoms of AF. Although the surgical maze procedure is very effective in preventing the recurrence of AF, the invasive nature of this procedure and some unanswered questions about the normalization of atrial function have rendered this therapy an uncommon choice for the initial nonpharmacological treatment of AF.

This review primarily discusses catheter ablation for AF, which has become an important option for treating patients with drug-refractory symptomatic AF. We have structured the discussion to provide specific information to nonspecialists who are advising or examining a patient with AF.[141,142]

CARDIAC ABLATION FOR AF

Catheter ablation either heats (radiofrequency) or cools (cryothermy) the atrial myocardium to eliminate the arrhythmogenic tissue and thereby decrease the risk of AF.

During the past decade, the use of radiofrequency ablation to treat patients with symptomatic AF has increased greatly.[143] Two reasons account for this important advance. First, AF is not a homogeneous disorder: it includes paroxysmal forms, in which a distinct trigger may be identified, and chronic forms, in which the atrial myocardial substrate is normal. Second, the thoracic veins play an important role in initiating AF (Figure 5).[144] For many decades, AF was thought to be a result of meandering wavelets of reentry that themselves result from a diseased atrial myocardium.[145,146] Although this is still relevant for persistent AF, in the past decade distinct triggers for AF have been found to arise from the myocardium of the pulmonary veins and other thoracic veins[8,147-149] (Figure 6).

Pulmonary Vein Isolation

The most common type of ablation for AF involves electrical isolation of a pulmonary vein (Figure 7). The pulmonary veins are electrically active structures with a sleeve of syncytial myocardium that extends from the atrium into the vein.[150] Electrical isolation involves placing a series of circumferential ablation lesions into the left atrium around the ostia of the pulmonary veins. Such circumferential isolation electrically disconnects the pulmonary veins from the rest of the atria. The rationale for this procedure is that electrical isolation of the veins renders the AF triggers that arise from those veins incapable of initiating arrhythmia in the atria.

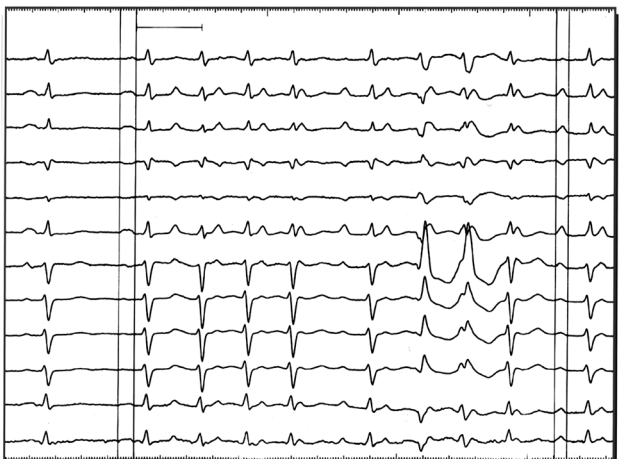


FIGURE 5. Although the electrocardiography of atrial fibrillation is generally straightforward, the onset of arrhythmia (premature atrial contractions or monomorphic atrial tachycardia) should be determined because of the importance of triggers for atrial fibrillation. Such a determination may help guide physicians in counseling patients about atrial fibrillation ablation.

During the typical pulmonary vein isolation procedure, a mapping catheter is placed into the pulmonary vein, and the characteristic abnormal signals from an arrhythmogenic vein are documented. The end point for ablation around that vein is the abolition of these abnormal signals, which signifies electrical disconnection of the vein from the atrium.

Nonpulmonary Vein Triggers

Not all initiators of AF arise from the pulmonary veins; any intrathoracic vein can potentially serve this function. The other common trigger sites are the myocardium that extends both into the vein of Marshall and into the superior vena cava. The vein or ligament of Marshall in the adult is a remnant of the left superior vena cava, which is present in the developing fetus but typically regresses before birth.[141,142,151] These venous structures can also be electrically isolated using a procedure similar to that described for the pulmonary veins.[152]

Substrate-Based Ablation Approaches

Ablation targeting the triggers of AF is the most common approach, but it is primarily effective for patients with paroxysmal AF and normal atria (substrate). Ablation is of minimal value for patients with the AF triggers of cardiac disease; diastolic dysfunction; valvular disease; or enlarged and abnormal, possibly fibrotic, atria. For these patients, relief is provided by various approaches aimed at ablating the abnormal substrate.

The most common of these evolving ablation techniques is linear ablation, which anchors the pulmonary vein isolation circle to other ablation sites or to the mitral

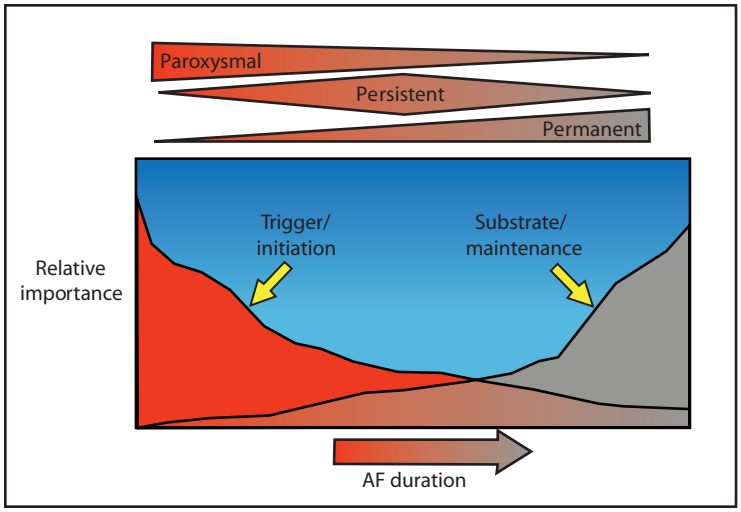


FIGURE 6. Paroxysmal atrial fibrillation (AF) can be a very different disease from permanent or chronic AF. Triggers are important for initiating paroxysmal AF, whereas substrate abnormalities are necessary for maintaining permanent AF. Although the natural history of paroxysmal AF is not exactly known, many patients will progress to the more permanent form.

valve. The goal of this linear ablation is similar to that of the surgical maze procedure: preventing the development of macroreentrant left atrial flutter. In addition, this substrate reduction (again as in the maze procedure) may decrease the likelihood that AF will develop or be sustained.

Another ablative approach targets high-frequency left atrial activity that manifests itself by the recording of multiple very rapid fractionated electrograms. Ablation has been performed at these characteristic sites.[153] Currently, it is unknown whether this ultrarapid activity results from areas of abnormal conduction, intrinsic rotors, neural

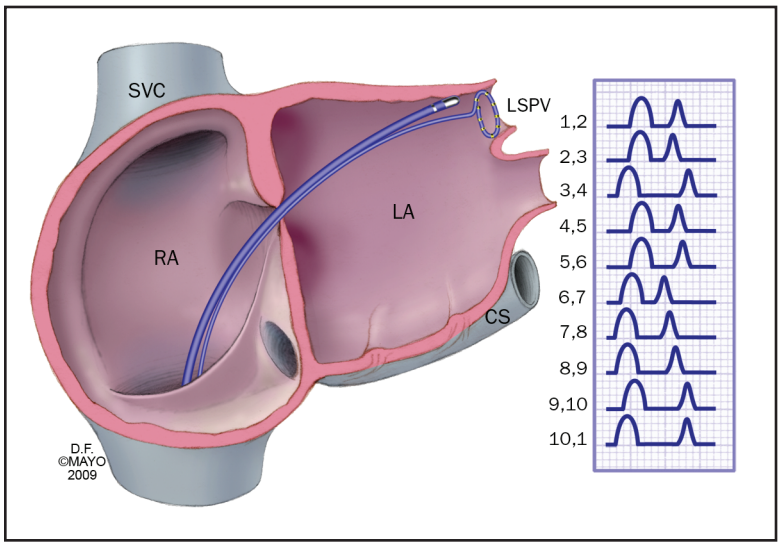


FIGURE 7. Pulmonary vein isolation is currently the most common ablation technique used for atrial fibrillation. The typical placement of a circular mapping catheter within the pulmonary vein is shown. Importantly, the ablation catheter and the delivery of energy are placed outside the vein within the left atrium. Also pictured are the characteristic intracardiac electrograms from an arrhythmogenic vein. After successful isolation of the vein, these electrographic abnormalities will disappear. CS = coronary sinus; LA = left atrium; LSPV = left superior pulmonary vein; RA = right atrium; SVC = superior vena cava.

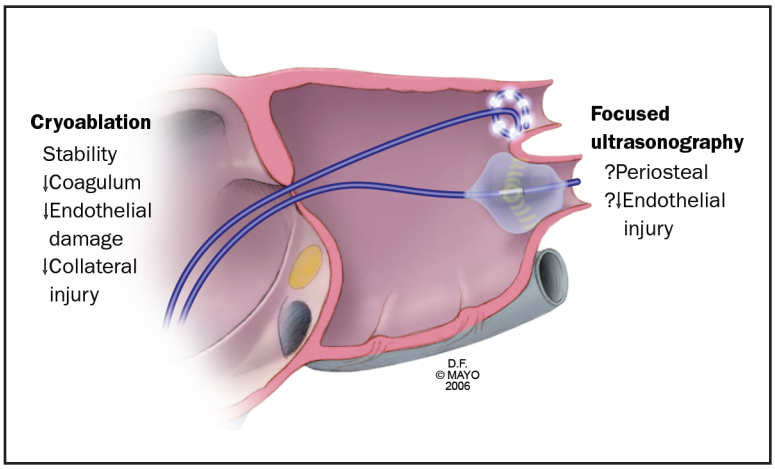


FIGURE 8. Newer techniques for atrial fibrillation ablation include the use of cryoablation rather than the thermal injury from radiofrequency energy. Balloon catheters and focused ultrasonography are also being investigated to facilitate faster, more effective, and safer left atrial ablation for atrial fibrillation. ↓ = decreased; ? = potential.

activity, or microreentry.[154] Newer energy sources, including cryoablation and focused ultrasonography, may potentially facilitate venous isolation along with local substrate modification and transmural ablation of epicardial innervation (Figure 8).

An exciting new approach targets the action of the atrial parasympathetic and sympathetic nerves.[33,155,156] The ganglionated plexuses are located along the posterior and superior portions of the left atrium. Recently, clinicians have adopted the use of ablation at these locations with local stimulation for identifying the presence of these ganglia.[33,155] Catheter ablation at these sites alters parasympathetic activity, as reflected by changes in heart rate variability,[128,157] and may decrease the ability of the atria to maintain AF.

Success Rates

Early reports describe success rates of 22% to 85% for ablation as a treatment for AF; relatively higher success rates are achieved for patients with paroxysmal AF.[158,159] Long-term results are limited because follow-up has generally been no longer than 1 year in randomized trials comparing the effectiveness of pulmonary vein isolation and drug therapy for patients with symptomatic AF. The reported success rates with this limited follow-up period ranged from 31% to 88%; neither strategy was clearly superior.[160,161] Generally, patients are informed that the success rate is approximately 60% to 70%, that approximately 10% to 40% of patients require a second procedure, and that 10% to 15% require continued antiarrhythmic therapies. These results are based on average outcome reports from multiple studies.[8,147,162-166]

Available findings also indicate that ablation is less effective for chronic AF than for paroxysmal AF. Several studies have reported these lower success rates even with more aggressive ablation paradigms.[167-169] Recently, the use of extensive linear ablation aimed at organizing and subsequently eliminating chronic AF achieved slightly better results but with a limited follow-up period[168,169] (Figure 9).

Thus, when counseling patients, clinicians must emphasize the fact that long-term cure rates are currently unknown but that approximately 60% to 70% of patients experience marked reduction or elimination of AF. Multiple single-center studies have shown substantial improvement in patients' quality of life after primary ablative intervention.[170-172] Several comparative studies found that quality of life after ablation is comparable with that of healthy persons not undergoing ablation.

Although much information is available about the effectiveness of ablation for individual patients, findings about the cost-effectiveness of this intervention are just beginning to emerge. A French study has shown that the cost of ablation is lower than that of pharmacological intervention.[173] However, this finding may not apply to the US health care system.

Complications

Serious complications may occur as a direct result of AF ablation procedures. Many of these complications are similar to those associated with other catheter-based interventions, such as infection, bleeding, hematoma, deep venous thrombosis, pneumothorax, and arterial damage.[165] Fortunately, more serious complications are rare: early

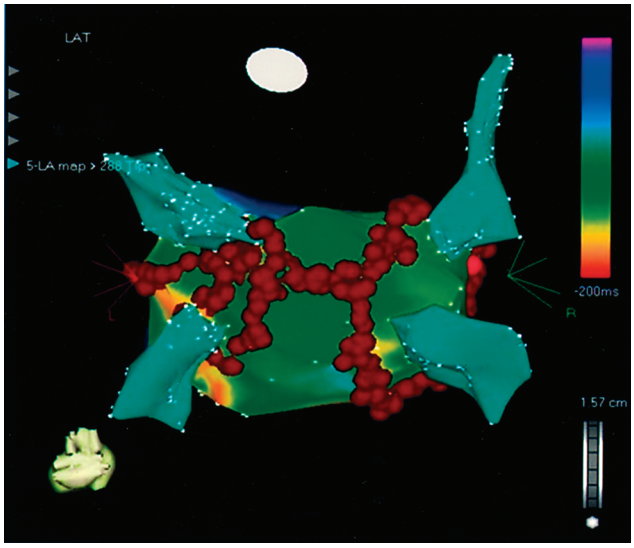


FIGURE 9. Current ablation approaches for patients with persistent atrial fibrillation include pulmonary vein isolation and linear ablation in the atrium, which connects ablation sites from the vein with each other and with the mitral annulus (red dots). Thus, a combined approach aimed at modifying abnormal substrate and eliminating common triggers is used. Linear ablation is primarily performed to prevent macroreentrant atrial tachycardia, including atypical atrial flutter.

studies show a rate of 0.5% to 1.0% for air emboli, bradycardia, tamponade, and stroke or TIA. These numbers have been confirmed by the more recent International AF Ablation Registry.[143]

Some complications, however, are relatively specific to AF ablation procedures. These include pulmonary vein stenosis, thromboembolic events, and the formation of atrial esophageal fistula.

Pulmonary Vein Stenosis. Ablation within a pulmonary vein can lead to fibrosis and narrowing or occlusion of the vessel.[174,175] Studies conducted before 2002 documented rates of pulmonary vein stenosis ranging from 4% to 10%.[176-178] If the ostium of the pulmonary vein is clearly recognized and ablation within the pulmonary vein is avoided, this complication is rare (Figure 10). Symptoms of stenosis include shortness of breath and, in severe cases, hemoptysis or pulmonary hypertension. Symptoms decrease over time; when they are severe, pulmonary vein dilation or stenting can be performed.[174,179]

Thromboembolic Events. Available studies document a rate of stroke ranging from 0.5% to 2.0% with ablative intervention; this rate is similar to that associated with other procedures currently used to treat AF.[143,165] Early heparinization, the use of intracardiac ultrasonography, and aggressive anticoagulation regimens appear to have reduced the incidence of this complication.[180]

Left Atrial-Esophageal Fistula. A potentially catastrophic consequence of AF ablation is the formation of a fistula between the posterior left atrium and the esophagus. This complication was first reported in 2004; since then, a number of similar cases have been reported.[181-184] This fistula produces a serious syndrome with fevers, odynophagia, gastrointestinal bleeding, and central nervous system manifestations, which are in part related to air emboli, as well as high fatality rates. Patients occasionally survive when surgery or another invasive intervention is performed promptly.[181,185]

When Ablation Fails to Control Symptoms

As previously noted, although AF ablation is an important advance in the management of patients with symptomatic AF, success is far from sure: at least 30% to 40% of patients continue to experience symptoms after a single procedure. The current treatment approaches for this patient group include another attempt at AF ablation, the combination of ablation with an antiarrhythmic therapy that may have

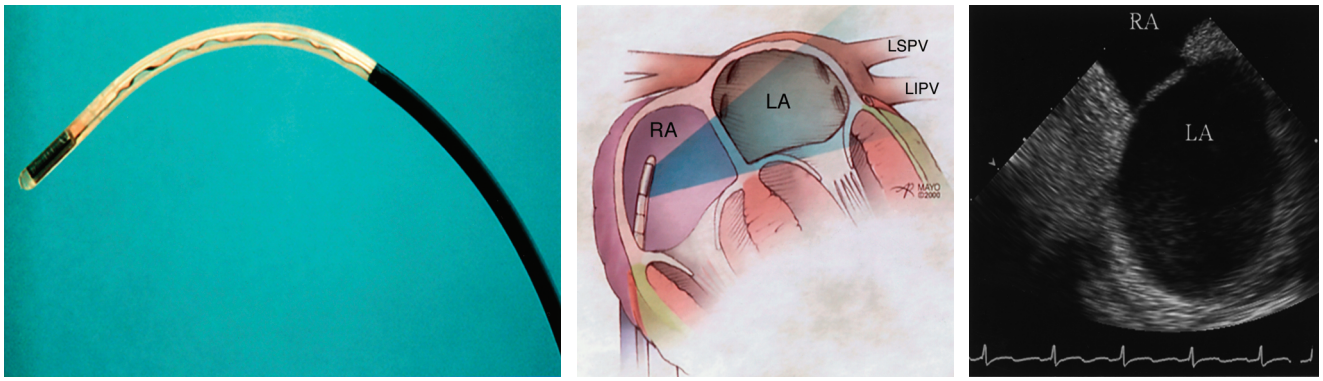


FIGURE 10. Intracardiac ultrasonography has substantially facilitated radiofrequency ablation procedures. Left, Linear phased array probe. Middle, Placement of the probe in the right atrium (RA) allows visualization of the left atrial pulmonary vein orifices (right) without the need for placing another catheter in the left atrium (LA) itself. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein.

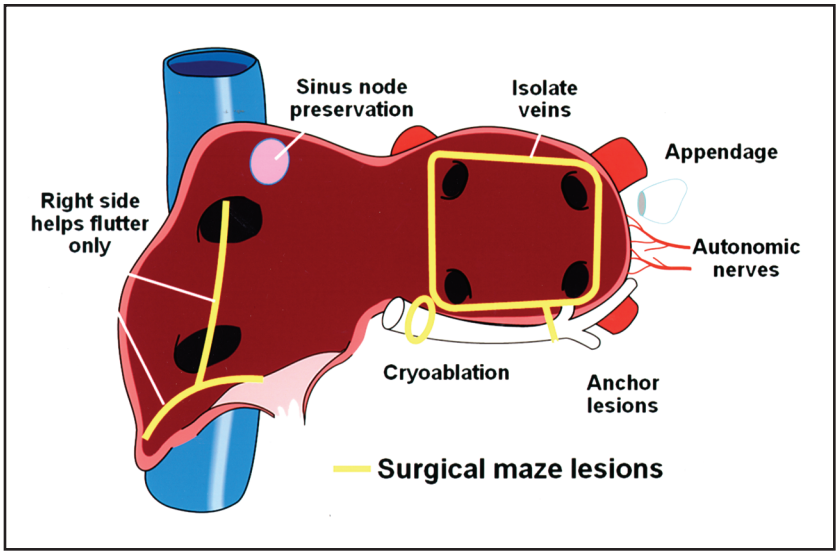


FIGURE 11. Atrial fibrillation (AF): lessons from the operating room. Current endovascular AF ablation has in many ways benefitted from the surgical experience with managing AF. Isolating the pulmonary veins, anchoring lesions (linear ablation), and understanding the role of eliminating the left atrial appendage or modifying the autonomic nerves are lessons learned directly from surgical experience.

failed previously, and the adjunctive use of antitachycardia pacing devices to terminate atrial flutter, which may persist after AF ablation.

The surgical maze procedure is still the most effective invasive therapy for AF ablation (Figure 11). Because of its invasive nature, and because recently developed techniques involve simpler procedures, it is rarely adopted as a first-line treatment. Patients with symptomatic chronic AF for whom medical and ablation attempts have failed may be considered for this treatment option.

Patient Selection for AF Ablation

For patients who continue to exhibit symptoms after an attempt at controlling ventricular response rates, interventions aimed at maintaining sinus rhythm should be attempted. If at least 1 attempt at AAD therapy has failed (intolerance or inefficacy), AF ablation is typically recommended. The ideal patient is a young and otherwise healthy person without structural heart disease who has paroxysmal AF. The success rates associated with ablation for such patients are substantially higher than those associated with ablation for patients with chronic AF and structural heart disease. For paroxysmal AF, if monitoring has shown a reproducible incitation of AF episodes with a single premature beat, the success rate of pulmonary vein isolation is likely to be high.

Additional trials are necessary to assess the effect of ablation on long-term outcomes. The Radiofrequency Ablation for Atrial Fibrillation Trial (RAAFT), which is currently under way, will better assess the late recurrence rates of AF.[127] The effect of ablation on mortality rates, quality of life, and health care costs will probably be better established during the coming years. The CABANA (Ablation vs Drug Therapy for Atrial Fibrillation) pilot study, which is currently under way, will be followed by a 3000-patient CABANA mortality trial, in which 1500 patients older than 65 years or younger than 65 years but with other risk factors for stroke will be randomly assigned to drug therapy, and an additional 1500 such patients will be randomly assigned to ablative intervention. This study will probably require approximately 6 years for completion but should provide important information about the effectiveness, safety, and long-term consequences of current ablative therapies.

CONCLUSION

Atrial fibrillation is the most common arrhythmia seen in clinical practice; therefore, all health care professionals should be familiar with the appropriate management of AF. The past decade has witnessed important changes in the management of symptomatic AF with the advent and increasing adoption of invasive therapies, specifically AF ablation. We have presented an approach that should aid the nonspecialist in recognizing which patients are likely to benefit from newer therapies and in understanding the

rationale, techniques, success rates, and limitations of ablation that are pertinent to the appropriate counseling of patients with AF.

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