# Modern Trends in the Management of Atrial Fibrillation

*Atrial fibrillation is the most common cardiac arrhythmia and leads to an increased risk of stroke, heart failure, and death in affected patients. Despite a plethora of treatment modalities and many advances in our understanding of atrial fibrillation mechanisms and natural history, the management of patients with atrial fibrillation continues to pose many challenges. This review provides a concise discussion on the role of various pharmacologic and nonpharmacologic therapies that are currently being utilized. The recommendations are evidence based and take into account the findings of many recently conducted outcome trials in atrial fibrillation.*
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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and affects about 2.2 million people in the United States.[1–4] Its prevalence is age-dependent and the vast majority of affected patients are elderly. The presence of AF increases mortality risk by two-fold and stroke risk by five-fold.[3–5] Patients with AF experience symptoms due to the rapid and irregular nature of the ventricular rhythm and the loss of atrial contraction.

The approach to AF has undergone dramatic changes in the last decade and its management has been greatly facilitated by the recently published guidelines endorsed by the American College of Cardiology, American Heart Association, and European Society of Cardiology.[6] Experimental and electrophysiologic studies[7–12] have provided new insights into the mechanisms behind initiation and perpetuation of AF. Prospective randomized trials[13–24] have furnished more definitive data regarding the risk-benefit analysis of the various anticoagulants and antiarrhythmic drugs. Recently available data from two large trials[25,26] provide an evidence-based approach in regard to the strategies of rhythm vs. rate control. Finally, nonpharmacologic modalities are assuming a greater role in the management of AF[27–29] and it has become possible to cure AF by radiofrequency (RF) ablation of the tissue in or close to the pulmonary veins.[30,31]

## Classification of AF

Previous classification schemes have largely been abandoned in favor of the new scheme that classifies AF into three types: paroxysmal, persistent, and permanent.[6] *Paroxysmal* AF refers to the episodes that terminate spontaneously in less than 7 days. *Persistent* AF refers to the episodes that don't spontaneously terminate but can be converted to sinus with pharmacologic or electrical cardioversion. *Permanent* AF refers to the long-lasting state of AF that cannot be terminated or is only transiently terminated by chemical or pharmacologic means.

## Pathophysiology and Electrophysiologic Mechanisms

A considerable body of evidence supports the assertion that AF is caused by multiple reentry waves that

**Table I.** Initial Approach to a Patient With Atrial Fibrillation (AF)

| |
|---|
| Classify AF: paroxysmal, persistent, or permanent; new onset or indeterminate origin |
| Hemodynamic tolerance and symptom profile of the arrhythmia |
| Determine the cause of AF |
| Define the type and severity of underlying heart disease |
| Identify other extracardiac conditions and transient precipitating factors |
| Risk assessment for thromboembolism, drug proarrhythmia, and hemorrhagic complications of the anticoagulants |
| Need for hospitalization |

propagate around the atrial tissue in a random fashion.[10,11] During propagation, the wave-fronts may fractionate into daughter wavelets, of which some get self-extinguished but others perpetuate. The likelihood of perpetuation is higher if the circulating wavefronts are of short wavelength (a product of conduction velocity and effective refractory period) and are greater in number (typical range 3–6). Such a reentrant milieu is likely to occur in the atria with structural abnormalities that accompany aging or occur as a result of associated cardiovascular abnormalities including atrial dilatation, hypertrophy, fatty infiltration, patchy fibrosis, or amyloid deposits.[6,7]

Recent observations have implicated a focal origin of AF, especially in a select subset of patients with paroxysmal AF.[12] Several investigators have demonstrated the presence of one or more rapidly firing atrial foci that are located just within or around the periostial region of the pulmonary veins and can induce AF in susceptible individuals.[12,30,31] RF ablation of such foci may lead to the cure of AF in such patients. Whether the pulmonary vein foci contribute to the initiation and maintenance of persistent or permanent AF remains to be determined and is an area of ongoing clinical investigation.

## Management of AF

As the AF cure remains elusive, management strategies are essentially palliative and preventive in nature. The goals of management are to restore and maintain the sinus rhythm, achieve an adequate control of the ventricular rate, and prevent thromboembolic episodes. Given the vast etiology of AF and its varying clinical manifestations, no single strategy exists that is suitable for each patient with AF.

Table I outlines the steps needed in the initial evaluation of a patient with AF. This evaluation should include a careful history and physical examination, serum chemistry including thyroid functions, chest x-ray, 12-lead electrocardiogram, and two-dimensional echocardiography. A more detailed investigation may include Holter monitoring, transesophageal echocardiography (TEE), stress testing, or electrophysiologic testing. Once AF is well characterized in regard to its temporal pattern, etiology, and clinical manifestations, it becomes easier to formulate an effective management strategy from a myriad of available therapeutic options (Table II).

**Table II.** Management Strategies in Atrial Fibrillation (AF)

| Strategy | Pharmacologic Options | Nonpharmacologic Options |
|---|---|---|
| Rate control | Digoxin, calcium channel blockers, β blockers | AV nodal ablation or modification and permanent pacemaker |
| Rhythm control | Class Ic (flecainide, propafenone) | Surgical maze |
| | Class Ia (quinidine, procainamide, disopyramide) | Catheter maze |
| | β Blockers | Pulmonary vein isolation |
| | Class III (sotalol, amiodarone azimilide, dofetilide) | Focal "trigger" ablation |
| | | Dual chamber pacing, atrial defibrillators |
| Prevention of thromboembolism | Aspirin<br>Warfarin | LA appendectomy<br>Percutaneous LA appendage occluding devices |

AV=atrioventricular; LA=left atrial

**Table III.** Antiarrhythmic Agents for Pharmacologic Conversion of Atrial Fibrillation (AF)

| Drug | Route of Administration | Typical Dose | Relative Efficacy* |
|---|---|---|---|
| Ibutilide | IV | 1–2 mg bolus | 30%–60% |
| Procainamide | IV | 10–15 mg/kg bolus | 20%–30% |
| | | 1–4 mg/min infusion | |
| Amiodarone | IV | 5 mg/kg bolus | 10%–30% |
| | | 0.25–1 mg/min infusion | |
| Diltiazem | IV | 10 mg bolus | 5%–10% |
| | | 5–10 mg/h infusion | |
| Quinidine | Oral | 1–2 g/d divided doses | 20%–50% |
| Flecainide | Oral | 300 mg single dose | 40%–60% |
| Propafenone | Oral | 450–600 mg single dose | 40%–60% |
| Sotalol | Oral | 160–320 mg/d divided dose | 30%–50% |
| Dofetilide | Oral | 500–1000 μg/d | 20%–30% |
| | | Divided doses | |

IV=intravenous; *estimates of the relative efficacy based on review of the literature

**Restoration of Sinus Rhythm.** The potential advantages of sinus rhythm restoration include preservation of atrial transport function, prevention of congestive heart failure progression, relief of AF-related symptoms, reduced risk of thromboembolic episodes, and improved survival. Sinus rhythm can be restored by antiarrhythmic drugs or synchronized direct current shock.

*Pharmacologic Cardioversion.* Pharmacologic cardioversion is likely to be effective for recent onset AF, especially when it occurs in the setting of no or mild structural heart disease. Table III outlines the list of drugs used for pharmacologic cardioversion of AF. Depending upon the AF duration, drugs are effective in 40%–80% of patients.[1,2,19] While evaluating drug efficacy, it should be emphasized that AF may convert spontaneously to sinus in up to 40% of the patients when the AF duration is less than 8 hours, and in up to 20% of the patients when the AF duration is less than 48 hours.[6] Spontaneous conversion is rare in AF of more than 7-days duration.

Pharmacologic cardioversion should always be performed in the hospitalized setting except for low-dose oral amiodarone, which may be administered on an outpatient basis.

*Electrical Cardioversion.* Electrical cardioversion is indicated for AF associated with hemodynamic compromise or when pharmacologic cardioversion is unsuccessful. It is performed under general anesthesia or deep conscious sedation, and entails delivery of a QRS synchronized direct current shock across the left precordium. Electrical cardioversion is successful in 80%–90% of patients.[14,32] For a given energy level, the rate of success is higher for the biphasic than the monophasic waveforms, and higher for the anteroposterior than the anterolateral paddle positions. Moreover, successful biphasic shocks produce fewer thermal skin burns and require half the energy output of an equivalent monophasic shock.[33] In patients with failed cardioversion, pretreatment with intravenous ibutilide or oral sotalol lower the energy requirement for atrial defibrillation and may thus facilitate cardioversion.[6] Infrequently, internal cardioversion may be needed to restore sinus rhythm.

*Anticoagulation Prior to Cardioversion.* Careful attention to anticoagulation before cardioversion is critical because thromboembolic events may complicate cardioversion in 1%–7% of patients who are not anticoagulated or are underanticoagulated.[32,34] Thromboembolic events occur with both chemical or electrical cardioversions and, thus, anticoagulation recommendations are the same for both means of cardioversion.[6]

For AF of less than 48-hours duration, precardioversion anticoagulation is not required. After cardioversion, oral anticoagulants may be needed in

**Table IV.** Antiarrhythmic Drugs for Maintenance of Sinus Rhythm in Patients With Atrial Fibrillation (AF)

| Drug | Class of Drug | Daily Dose | Relative Efficacy** |
|---|---|---|---|
| Procainamide | Ia | 1000–4000 mg | 10%–30% |
| Quinidine | Ia | 600–1600 mg | 30%–40% |
| Disopyramide | Ia | 300–900 mg | 20%–40% |
| Flecainide | Ic | 200–400 mg | 40%–50% |
| Propafenone | Ic | 450–900 mg | 40%–50% |
| Sotalol | III | 160–480 mg | 40%–50% |
| Dofetilide | III | 500–1000 μg | 40%–50% |
| Azimilide* | III | 75–125 mg | 40%–50% |
| Amiodarone | III | 200–400 mg | 50%–70% |

*Investigational; **estimates of relative efficacy based on review of the literature

those who are likely to have recurrent AF or deemed to be at high risk for thromboembolic events.

In patients with AF of more than 48-hours duration, or of unknown duration, an adequate anticoagulation (international normalized ratio [INR], 2.0–3.0) for 3–4 weeks before cardioversion is necessary.[6] When the need for cardioversion is more immediate, a TEE-guided approach may be used. This entails administration of intravenous heparin or subcutaneous low molecular weight heparin for 24 hours followed by TEE. If TEE shows no left atrial thrombus, electrical cardioversion may be safely accomplished, as the subsequent thromboembolic risk is low at less than 0.5%.[34] After cardioversion, oral anticoagulation should be continued for 4 weeks or longer, depending on the intrinsic risk for thromboembolic events in a given patient.

**Maintenance of Sinus Rhythm.** After restoration of sinus rhythm, if no antiarrhythmic prophylaxis is given, AF will recur in up to 20% of the patients in the first 48 hours and in another 20%–30% within 2–4 weeks of follow-up. At 1 year, less than 10% of the patients remain in sinus rhythm.[14,15] Similarly, in patients with paroxysmal AF, AF is likely to recur in all cases, except when it was caused by reversible and transient factors. Thus, if maintenance of sinus rhythm is a desired goal of treatment, antiarrhythmic drug prophylaxis will be needed in most patients.

Table IV lists various antiarrhythmic drugs in use to prevent recurrence of AF. Except amiodarone, other antiarrhythmic drugs have comparable efficacy of 30%–50% at 1–2 years of follow-up.[2,6,19] The comparable efficacy of three antiarrhythmic drugs was prospectively evaluated in a recently published Canadian study[21] where 403 patients with paroxysmal AF were randomized to sotalol, propafenone, and amiodarone. At 6-month follow-up, AF suppression was achieved in 65% of patients receiving amiodarone compared with 37% of those receiving sotalol or propafenone ($p<0.001$).[21]

While selecting an antiarrhythmic drug for AF prophylaxis, the following considerations should be emphasized. First, antiarrhythmic drugs may not be needed in a select subset of patients with first onset AF occurring in the setting of no structural heart disease or in those with infrequent and well-tolerated episodes.[6] Second, the decision-making process regarding drug selection is guided more by the drug safety profile and the type and severity of the underlying heart disease than by any significant differences in the drug efficacy (Table V). Class Ic drugs have a high safety profile in patients without structural heart disease[18] and are thus considered first-line drugs in such patients. However, their proarrhythmic risk is relatively high in patients with coronary artery disease or congestive heart failure and they are thus contraindicated in such patients.[2,19] The use of sotalol is safe and associated with low proarrhythmic potential in patients with heart disease or coronary artery disease and it is the drug of first choice in these patients.[17,19] However, its proarrhythmic potential is high in patients with borderline prolonged QTc interval, female sex, or systemic hypertension, and it should be used with caution in such situations. In patients with heart failure, an increased mortality risk has been associated with the use of almost all antiarrhythmic drugs except amiodarone[23] and dofetilide,[22] which have been shown to be mortality neutral and are, thus, the recommended drugs of choice in patients with heart failure and AF.

Third, recurrence of AF should not be equated with drug failure and the goal of treatment should be

**Table V.** Antiarrhythmic Drug Selection to Maintain Sinus Rhythm in Patients With Atrial Fibrillation (AF)*

| | Lone AF | CAD | SHD Present Hypertension** | CHF |
|---|---|---|---|---|
| First-line drugs | Flecainide | Sotalol | Flecainide | Amiodarone |
| | Propafenone | | Propafenone | Dofetilide |
| | Sotalol | | | |
| Second-line drugs | Amiodarone | Amiodarone | Amiodarone | |
| | Dofetilide | Dofetilide | Dofetilide | |
| | | | Sotalol | |
| Third-line drugs | Quinidine | Quinidine | Quinidine | |
| | Procainamide | Procainamide | Procainamide | |
| | Disopyramide | Disopyramide | Disopyramide | |

SHD=structural heart failure; CAD=coronary artery disease; CHF=congestive heart failure; *recommendations based on American College of Cardiology/American Heart Association/European Society of Cardiology committee for practice guidelines[6]; **hypertension with left ventricular hypertrophy ≥1.4 cm: amiodarone first-line drug

to produce a significant reduction in the AF burden rather than its complete suppression. Frequently, when a single drug is ineffective, addition of β blockers provides synergistic effects. At other times, a second or third drug with different antiarrhythmic mechanisms may be more effective. Infrequently, the drug selection may also be influenced by the underlying mechanism of AF. Vagomimetic AF often responds to disopyramide while the β blockers may be more effective for adrenergic-driven AF.[9]

Finally, the clinician faces an important dilemma on when to hospitalize a patient for the initiation of antiarrhythmic drugs.[6,24] Inhospital initiation is recommended when the patients have one or more of the following conditions: structural heart disease, sick sinus syndrome, atrioventricular (AV) conduction disorders or bundle branch block, prolonged QTc, electrolyte imbalance, or significant hepatic or renal disease. It is safe to administer class Ic drugs on an outpatient basis when the patient has none of the aforementioned conditions. Sotalol may also be administered on an outpatient basis to patients without any known risk factor for torsades de pointes.[6] However, it is a good policy to start at the lower dose range, and any increment in the dose should be made only under very careful outpatient clinical and electrocardiographic monitoring. It is also safe to administer low-dose amiodarone on an outpatient basis.[20]

**Maintenance of Ventricular Rate Control.** In AF patients with rapid heart rate, control of the ventricular rate is essential to relieve AF-related symptoms and to prevent progression to tachycardia-related cardiomyopathy. For rate control, the target resting heart rate is 60–80 beats/min, with rate increasing to 90–120 beats/min during moderate exercise.[6,25] Intravenous diltiazem and esmolol are the drugs of choice when a rapid control heart rate is the desired goal. Intravenous verapamil, propranolol, or metoprolol are other alternative choices.[2,19] Intravenous digoxin is less effective; its effects do not manifest for the first 2–4 hours despite an aggressive dose-loading schedule. However, in patients with heart failure, intravenous digoxin is considered the drug of choice for rate control because of its safety profile.[6]

In patients with persistent or permanent AF, the heart rate control is achieved and maintained by the use of oral AV nodal slowing agents. These drugs include digoxin, β blockers, and calcium channel blockers and may be used alone or in combination, to achieve an optimum heart rate control both at rest as well as during exercise. In some patients, especially those with sick sinus syndrome, symptomatic bradycardia may develop during attempts at heart rate control and these patients may require permanent cardiac pacing.

**Prevention of Thromboembolism.** In patients with AF, the substrate for thrombus formation is provided by the loss of organized atrial contraction and decreased atrial blood flow velocity.[5,8] Left atrial thrombus is reported to be present in 10%–15% of patients during TEE[34] or postmortem studies and the left atrial appendage is the most common site for thrombus formation. Consequently, patients with AF face an increased risk for embolic complications.

**Table VI.** Risk Stratification for Thromboembolic Episodes in Atrial Fibrillation*

| Clinical Risk Factors | Echocardiographic Risk Factors |
|---|---|
| Previous stroke or TIA | LA enlargement |
| History of hypertension | Left ventricular dysfunction |
| Heart failure | LA thrombus |
| Advanced age | Decreased LA appendage flow velocity |
| Coronary artery disease | High-density spontaneous contrast |
| Diabetes mellitus | |

TIA=transient ischemic attack; LA=left atrial; *based on the results of primary prevention trials in patients with nonvalvular atrial fibrillation

The results of five large randomized trials[1-3] have conclusively proved the effectiveness of adjusted-dose oral warfarin in reducing the risk of thromboembolic complications. A meta-analysis of these trials revealed that warfarin reduced the risk of stroke by 78% on treatment analysis and by 61% on intention-to-treatment analysis. The data for beneficial effect of aspirin are less convincing.[1,2,6]

The decision to institute warfarin or aspirin should consider the intrinsic risk for thromboembolic events and the frequency of bleeding complications from warfarin. Table VI lists the risk factors for thromboembolic episodes.[6] For patients under age 60 with no known risk factors, the risk of thromboembolic complications is less than 1% per year and aspirin prophylaxis may suffice. For patients between 60–70 years of age with no other known risk factors, aspirin and warfarin are of comparable efficacy and an individualized decision needs to be made in such patients. Adjusted-dose warfarin is the recommended regimen for patients aged 70 or greater, and for AF patients with one or more risk factors for thromboembolic episodes.

It should be emphasized that patients with atrial flutter also face an increased risk for thromboembolic episodes. Compared with AF patients, the magnitude of the risk is less but they should be risk-stratified using the same criteria.

The maximum protection against thromboembolic episodes is achieved by tailoring anticoagulation intensity to an INR range of 2.0–3.0. In elderly patients with high risk of bleeding, the optimum INR range may be 1.6–2.5. Also, recent data[1,6] have shown no benefit of combining low-dose warfarin with aspirin and this combination should not be used. Finally, although no definite data are available, low molecular weight heparin appears to be as effective as intravenous heparin and, hence, may be used interchangeably with heparin.

**Selection of Rhythm Control vs. Rate Control.** For many years, the rhythm-control strategy was believed to be superior to the rate-control strategy because restoration of the sinus rhythm bestows many potential benefits. However, up until recently, no study had compared these two strategies; thus, controversy had existed as to which of the strategies should be adopted in the management of patients with AF.

This issue has been addressed in two large multicenter randomized and prospective trials.[25,26] In the North American trial of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM),[25] 4060 patients with a minimum age of 65 years were randomized to receive either rhythm-control or rate-control therapy. All had, at least, one risk factor for stroke and none had any contraindication for dose-adjusted warfarin. The use of anticoagulation was encouraged in all, but could be discontinued in the rhythm-control group if sinus rhythm was maintained for at least 4 weeks on the effective drug.

During a mean follow-up of 3.5 years, sinus rhythm was maintained in 63% of the rhythm-control group and in 35% in the rate-control group. Despite a higher maintenance of sinus rhythm, the total mortality in the rhythm-control group was 24% compared with 21% in the rate-control group ($p=0.06$). Both groups experienced ischemic strokes at an equal rate of about 1% per year. Interestingly, about two thirds of the strokes occurred in patients who had discontinued warfarin or in whom the INR was subtherapeutic. Also, patients in the rhythm-control group needed to be hospitalized more often and experienced more drug-related adverse side effects.

This lack of superiority of the rhythm-control strategy was also demonstrated in a Dutch study[26] in which 522 patients with persistent AF were randomized to receive either the rhythm-control strategy (with electrical cardioversion followed by sotalol, flecainide, propafenone, or amiodarone) or the rate-control strategy (with AV

nodal slowing drugs). As in AFFIRM, the vast majority had one or more of the risk factors for stroke. During the 2.3-year mean follow-up, sinus rhythm was maintained in 39% of the rhythm-control group and in 10% of the rate-control group. Compared with the rate-control group, the rhythm-control group tended to have a higher prevalence of the mortality and morbidity composite end point (23% vs. 17%), and a higher frequency of thromboembolic complications (7.9% vs. 5.5%).

These two studies have important clinical implications. It is evident that both strategies are equally effective in the management of elderly patients with symptomatic paroxysmal or persistent AF. Both studies have highlighted the importance of continuing warfarin, even when sinus rhythm appears to be maintained. The persistence of an increased thromboembolic risk in such patients may be due to the fact that asymptomatic AF episodes may continue to occur despite an apparent maintenance of sinus rhythm. However, it should be emphasized that both trials excluded elderly patients with lone AF as well as younger patients with highly symptomatic AF and therefore their findings may not apply to such patients.

**Nonpharmacologic Modalities in AF.** Nonpharmacologic modalities are assuming a bigger role in the management of patients with drug refractory AF. As described below, several new modalities have been added in the past few decades.

*AV Nodal Ablation and Pacing.* RF ablation of the AV node combined with permanent pacing is an established and effective modality in AF patients who have uncontrollable rapid rates, despite the use of AV nodal-slowing medications.[28] Such patients are highly symptomatic and are at risk of tachycardia-related cardiomyopathy. AV nodal ablation combined with pacing has been shown to lead to a significant reduction in symptoms, an improvement in left ventricular function, and a better quality of life.[28] The disadvantages include the long-term need for warfarin and permanent dependency on the pacemaker.

*Atrial Pacing.* In patients with sinus node dysfunction, atrial-based pacing has been shown to reduce the frequency of paroxysmal AF.[27] Another advantage of atrial pacing lies in its ability to alleviate the drug-induced bradycardia and, hence, optimize the dose of antiarrhythmic drugs. Sophisticated and complex atrial pacing algorithms have been devised, which along with multisite atrial pacing, may find utility in the treatment of symptomatic paroxysmal AF even in the absence of concomitant sick sinus syndrome.[29]

*Atrial Defibrillators.* Internal atrial defibrillators represent an attractive modality in a very small minority of patients with infrequent but poorly tolerated AF episodes that require hospitalization and electrical cardioversion.[29] In addition to atrial defibrillation, atrial defibrillators also possess the capabilities of dual-chamber pacing and sensing, sophisticated atrial overdrive pacing algorithms for AF prevention, and antitachycardia atrial pacing algorithms to terminate atrial flutter and fibrillation. The shocks for AF may be delivered in an automatic mode, but are preferably programmed in a patient-activated mode.

*Surgical Maze Procedures.* AF can be cured surgically by placing multiple incisions in or around the critical tissues and zones in the atria so as to create permanent barriers to the reentrant conduction, and hence inhibit AF. This procedure, known as surgical maze, is successful in more than 90% of patients.[35] It may be performed as an isolated procedure in patients with lone AF or in combination with other cardiac surgery for concomitant valvular ischemic or congenital heart disease. The surgical procedure entails excising both atrial appendages, encircling the pulmonary veins and placing the connecting lesions at the roof of the left atrium and mitral annulus, and creating an intercaval incision and cavo isthmus incision in the right atrium. The operative morbidity and mortality, although low, makes it an unattractive option in patients with lone AF. However, surgical maze should be considered in patients with symptomatic AF who are undergoing concomitant heart surgery for other cardiac conditions.[6]

*RF Catheter Ablation.* Initial attempts to cure AF by RF catheter ablation mirrored the surgical maze. Several investigators placed multiple linear lesions in the right atrium, left atrium, or both. Although AF was reported to be cured in 30%–70% of cases, the catheter-based Maze techniques have largely been abandoned due to their prolonged procedure durations and a relatively high incidence of complications.

Recent approaches to catheter ablation of AF have centered on the techniques of focal pulmonary vein ablation[12] and pulmonary vein isolation.[29,30] Haissaguerre et al.[12] were the first to report the presence of AF triggers in the pulmonary veins of over 90% of the patients with drug refractory paroxysmal AF. Focal RF ablation of these triggers led to an acute cure of AF in the vast majority, but 30% experienced recurrence during a follow-up of 6 months. Others[30,31] have reported similar experiences. One of the reasons for high recurrence is now recognized to be the presence of multiple (active or quiescent) foci within the same or the other pulmonary veins. Thus, the current approach is to

disrupt the electrical connection between the left atrium and the target pulmonary vein by delivering RF energy circumferentially around the pulmonary vein ostium (pulmonary isolation technique). Using this approach, the initial results have been promising with cure rates of 70%–80% for paroxysmal AF and 30%–40% for persistent AF.[30,31] The serious complications may occur in less than 1%–2% of the patients and include pericardial tamponade, cerebral ischemic events, phrenic nerve paralysis, and pulmonary vein stenosis.

## Conclusions

As a result of many advances made in the past few decades, we now have a better understanding of the mechanisms of AF. Based on the results of randomized controlled trials, it is possible to formulate optimum treatment strategies for patients with AF. The treatment strategies are increasingly becoming evidence-based and the maintenance of anticoagulation has become a critical component of the overall management. Clinical trials have also proved that there are no mortality or stroke reduction benefits with the rhythm-control over the rate-control strategy. Finally, it has become feasible to cure a select subset of patients with AF by RF-guided pulmonary vein isolation. This curative modality is likely to assume a greater role in AF management as the evolving technology becomes more sophisticated.

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# The Treatment of Patients With Hypertension and Ischemic Heart Disease

*The prevalence of coronary artery disease has not significantly declined in the past 30 years, and approximately only one in four patients with hypertension is treated to recommended blood pressure levels. Hypertension is a common antecedent of acute myocardial infarction and the association of the two conditions imparts a high risk. Many studies have indicated the benefit of β blockade, angiotensin-converting enzyme inhibition, antiplatelet therapy, and cholesterol-lowering therapy in patients with coronary artery disease with or without heart failure. All four classes of agents are needed in a large proportion of patients with this condition. In the treatment of uncomplicated hypertension, recent data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and second Australian National Blood Pressure Study (ANBP2) suggest that diuretics and long-acting dihydropyridine calcium channel blockers may also be useful in the prevention of coronary events. However, a large body of information indicates the benefit of angiotensin-converting enzyme inhibitors, antiplatelet agents, β blockers, and hypolipemic agents in patients with established disease.*
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During the last 30 years much progress has been made in the treatment and prevention of cardiovascular disease. Age-adjusted coronary heart disease mortality has declined steeply (by approximately 50% between 1972 and 1994) and the prevalence of hypertension has decreased by over 40%—from 36.3% of the population in the first National Health and Nutrition Examination Survey (NHANES I), carried out from 1971–1974, to 20.4% in NHANES III, carried out from 1988–1991.[1] Nevertheless, the prevalence of coronary artery disease (CAD) in the community and the incidence of acute myocardial infarction (AMI) have not declined as sharply and pharmacologic therapy is employed only in approximately 50% of patients with hypertension. Patients with coexistent hypertension and CAD have very high risk of mortality and morbidity. Observational studies and retrospective analyses of clinical trials have shown an increased risk in patients with hypertension and myocardial infarction (MI) compared with those with MI but no history of hypertension. This association persists in multivariate analyses considering other risk factors of patients with AMI. For example, in the Trandolapril Clinical Events (TRACE) study[2] the adjusted risk ratio for death (MI patients with hypertension vs. MI patients without hypertension) was 1.14 (95% confidence interval [CI], 1.04–1.24) and this effect was more pronounced in patients aged ≤ 65 years. Thus, hypertension is a moderate risk factor for mortality in patients after AMI and this increased risk is present at all levels of left ventricular systolic dysfunction. Angiotensin-converting enzyme (ACE) inhibitors, β blockers, and statins have been found to decrease the risk of morbid and mortal events in patients with hypertension and ischemic heart disease.

## Hypertension and Risk in Ischemic Heart Disease

Recently, particular emphasis has been placed on the physical, structural, cellular, and chemical characteristics of the "vulnerable or unstable plaques" prone to disruption and the genesis of acute coronary syndromes. The combination of plaque disruption and high thrombogenic systemic factors (e.g., catecholamines, plasminogen activator inhibitor (PAI), renin-angiotensin-system (RAS), fibrinogen) is more prevalent in hypertension. Fibrinolysis, fibrinogen, and PAI-1 may play a