

Atrial Fibrillation: The Nonpharmacologic Strategy

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Abstract

Pharmacologic treatment has been used for decades for conversion and prevention of recurrent atrial fibrillation (AF). But the use of antiarrhythmic drugs is associated with substantial side effects and mortality in some patients. Accordingly, it is not surprising that nonpharmacologic techniques have been developed for the management of AF, including the use of atrial defibrillators, atrial pacing methods, and several surgical and radiofrequency catheter ablation procedures.

The atrial defibrillator has been found to detect and treat atrial and ventricular arrhythmias appropriately, with successful termination of spontaneous AF through low energy shocks. Although these devices are promising, the factor which limits their widespread use is not safety or efficacy, but patient comfort. Several studies suggest that atrial-based cardiac pacing may have a beneficial effect in decreasing and preventing AF episodes in patients with sick sinus syndrome. Palliative ablative procedures also available for the treatment of atrial fibrillation include AV junctional modification and AV nodal ablation with permanent pacing, the latter technique being associated with improvements in ejection fraction.

Two potentially curative procedures are the surgical MAZE and endocardial catheter ablation. These techniques are based on placing strategically located lesions in the atrium to disrupt the conduction pathway(s). Recent studies have focused on ablative therapies aimed at the area of the pulmonic veins.

The main therapy for maintaining sinus rhythm after conversion is predominantly pharmacologic. Similarly, in the absence of heart block, if conversion to sinus rhythm is not successful, pharmacologic modalities may be required to control ventricular rate. In any case, planning a treatment regimen for the management of AF should include evaluation of the risks inherent in the use of various drugs as well as more invasive strategies.

Key Words: Atrial fibrillation, nonpharmacologic review management, catheter ablation maze.

Introduction

ATRIAL FIBRILLATION (AF) is the most common arrhythmia, with a reported prevalence of 1.9% for patients under 65 years of age, and 5%–6% of patients over age 65(1). The number of hospital admissions in the United States for AF has more than doubled from 1984 to 1994, from 111,000 to 270,000 (1). The morbidity and mortality of this arrhythmia may be attributed primarily to two factors:

- the propensity for thrombus formation with systemic thromboembolism such as stroke;

- the loss of atrial systolic function as a contributor to ventricular filling;

Many patients will become aware of palpitations due to the irregular rapid ventricular rate. To control these symptoms, improve functional capacity, and reduce the risk of embolism, it is common practice to restore sinus rhythm. However, atrial fibrillation may recur within three to six months in at least one half of treated patients (2).

Pharmacologic treatment has been used for decades for cardioversion and prevention of recurrent atrial fibrillation. But the use of antiarrhythmic drugs is associated with substantial side effects and mortality in some patients. Accordingly, it is not surprising that nonpharmacologic techniques have been developed for the management of AF, including external and internal electrical cardioversion, atrial pacing methods (3) to prevent AF, and several surgical (4) or radiofrequency catheter ablation procedures to cure AF (5).

As stated previously, the three therapeutic goals that should be considered for every pa-

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tient with AF are: (a) rate control, (b) maintenance of sinus rhythm, and (c) prevention of thromboembolism. The purpose of this article is to review the current nonpharmacologic strategies for rate control and maintenance of sinus rhythm in the management of AF (Table 1).

Pathophysiology

Electrophysiologic Mechanism of Atrial Fibrillation

Different nonpharmacologic treatment modalities are based on our understanding of the electrophysiology of AF. Data support the view that reentry is the primary mechanism of atrial fibrillation. More recent electrophysiological observations obtained during intracardiac radiofrequency catheter ablation of atrial fibrillation, however, support the ectopic-focus theory (6). These authors reported that they were able to terminate atrial fibrillation by applying discrete energy primarily within the area where the pulmonary veins enter the left atrium. This is important when understanding curative ablative therapy for AF, because these findings suggest that AF may arise from a focal area in the heart.

A key development in our understanding of the mechanism of atrial fibrillation was the multiple wavelet hypothesis of Moe (7). He noted that, "the grossly irregular wave front becomes fractionated as it divides about islets or strands of refractory tissue, and each of the daughter wavelets may now be considered as independent offspring. Such a wavelet may accelerate or decelerate as it encounters tissue in a more or less advanced state of recovery." Thus, the more wavelets present, the more likely the arrhythmia will continue. The number of wavelets depend on the atrial mass, re-

fractory period, and conduction velocity of various areas of the atria. In essence, a large atrial mass would favor an increase in the number of wavelets and sustained atrial fibrillation when the refractory period was short and conduction delayed.

The mechanism of initiation of atrial fibrillation is not certain in most cases, and is probably multifactorial. If we assume reentry to be the mechanism of atrial fibrillation, initiation requires an area of conduction block and a wavelength of activation short enough to allow the reentrant circuit in the myocardium. The normal aging process and coronary artery disease may result in anatomic changes that enhance homogeneity in conduction and thereby promote the probability of reentry (1).

Rate versus Rhythm

There are two established treatment strategies. One strategy is to restore and maintain sinus rhythm, and the other strategy is to control the ventricular response rate. In both strategies, adequate anticoagulation with warfarin therapy is important (8).

The potential advantages of suppressing AF and of maintaining sinus rhythm include a more physiologic control of heart rate, prevention of rate-related cardiac chamber dilatation, better exercise tolerance associated with the atrial contribution to cardiac output, and the possibility of reduced thromboembolic risk (9, 10).

The advantages of simply treating AF with optimal ventricular rate control and warfarin therapy include: avoiding potential proarrhythmic risks, including death, of antiarrhythmic drug therapy (11); avoiding other, less serious, adverse reactions to antiarrhythmic drugs; avoiding frequent recurrence of AF with rapid ventricular response; fewer compliance problems; and lower cost (12).

However, there has never been a large clinical trial with a head-to-head comparison of these two treatment strategies. It has always been postulated that since AF is associated with clot formation in the atria and stroke, maintaining sinus rhythm would obviate this risk (8). The AFFIRM trial (12), sponsored by the National Heart, Lung, and Blood Institute of the National Institutes of Health, addresses long-term treatment of either paroxysmal or persistent AF in patients at risk for systemic embolism or stroke. This study is designed to evaluate whether maintaining normal sinus

TABLE 1

Nonpharmacologic Therapies of Atrial Fibrillation

Palliative

Atrial Defibrillation
Atrial Pacing
Endocardial Catheter AV Nodal Modification
Endocardial Catheter AV Nodal Ablation with
Permanent Pacing

Curative

Surgical MAZE (multiple atrial incisions)
Endocardial Catheter Ablation
Catheter MAZE
Ablation of atrial fibrillation foci

rhythm or controlling the heart rate alone results in better survival for patients with atrial fibrillation. This trial will provide clinicians with important data to address some very relevant questions concerning the long-term treatment of AF. The focus of this study will not only be on mortality and morbidity, but also on the quality of life and cost effectiveness. The first patient was enrolled in November 1995 and follow-up is planned through April 2001.

Management of Atrial Fibrillation

Pharmacologic Therapy for Conversion and Maintenance of Sinus Rhythm

Patients who undergo a nonpharmacologic strategy for the management of AF probably have been treated with many medications that have either failed or become intolerable. These include quinidine, procainamide, disopyramide, propafenone, sotalol, flecainide, ibutilide, amiodarone and dofetilide (13–16). Few large, randomized clinical trials have assessed the efficacy of these agents in maintaining sinus rhythm. In one study, sotalol was just as effective as quinidine (17). Sinus rhythm was maintained in 50–60% of patients treated with propafenone, flecainide, or sotalol, often with fewer side effects than with quinidine (18–21). Amiodarone is considered by some to be the most effective agent for drug-refractory, symptomatic, recurrent AF, although very few prospective comparative drug data are available. According to recent studies, nearly two-thirds of patients treated remained in sinus rhythm for up to one-year follow-up (15, 16, 22–24). Frequent use of amiodarone for AF is

limited by its potentially severe and life-threatening side effects, which may be minimized with lower daily doses.

One recent study, the Canadian Trial of Atrial Fibrillation Investigators (25), found that amiodarone was more effective than sotalol or propafenone for the prevention of recurrences of atrial fibrillation. Of the 403 patients in the study, 201 were assigned to a regimen of amiodarone and 202 to one of either sotalol or propafenone. After a mean of 16 months of follow-up, 71 of the patients who were assigned to amiodarone (36%) and 127 of those who were assigned to sotalol or propafenone (64%) had a recurrence of atrial fibrillation ($p < 0.001$).

Ibutilide (26) is a class III (Table 2) antiarrhythmic drug, its predominant action being prolongation of the myocardial action potential duration. The mode of action is believed to involve activation of a late inward sodium current and possibly blockade of the rapidly activating component of the cardiac delayed rectifier potassium current (27). A review of 2 placebo-controlled trials involving 439 patients with sustained atrial flutter or AF reported that 33 to 49% of these patient converted to sinus rhythm after intravenous administration of ibutilide, 0.01 to 0.025 mg/kg or a total dose of 1 to 2 mg (28). In another trial involving 300 patients who developed atrial flutter or fibrillation after cardiac surgery, ibutilide, 2 mg, administered intravenously, successfully converted the arrhythmia in 57% of patients. The mean time to conversion was about 30 minutes in these trials (28). In another study, conversion to sinus rhythm occurred in 36 of 50 patients who had not received ibutilide (72%) whereas all 50 patients who had received ibutilide pretreatment

TABLE 2
Classification of Antiarrhythmic Drugs

Class	Action	Channel effect and/or ECG changes
I	Direct membrane action	Blocks fast sodium channels (Phase 0)
1a	Intermediate inhibition	Prolongs QRS and QT
1b	Less inhibition	Minimal effect of QRS and QT
1c	Marked inhibition	Prolongs QRS and QT
II	β -adrenergic blocker	Indirect closure of calcium channels (Phase IV); no effect on QRS and QT
III	Prolongation of repolarization	Blocks outward potassium channels (Phase III); prolongs QRS and QT
IV	Calcium channel blocker	Blocks slow inward (AV nodal) calcium channels (Phase II); no effect on QRS and QT

and external cardioversion converted to sinus rhythm ($p < 0.001$) (29). In 3 trials, ibutilide was significantly more effective than racemic sotalol or procainamide in terminating atrial flutter or fibrillation (13, 18, 26). Important side effects which must be monitored include: sustained polymorphic ventricular tachycardia, torsades de pointes, which developed in 1.7%, and non-sustained polymorphic ventricular tachycardia, which occurred in 2.7% of 586 patients treated with ibutilide in clinical trials. The drug has minimal hemodynamic effects and is associated with few noncardiovascular adverse events. Thus, ibutilide is a useful agent for the pharmacological cardioversion within 30 days of recent-onset atrial fibrillation or flutter, provided that adequate steps are taken to monitor for proarrhythmic events.

The Danish Investigations of Arrhythmia and Mortality on Dofetilide Study Group (30), found that dofetilide, a novel class III antiarrhythmic drug that selectively inhibits the rapid component of the delayed rectifier potassium current and prolongs the refractory period, was effective in converting atrial fibrillation and preventing its recurrence in patients with congestive heart failure. Of the 190 patients with AF at baseline, 22 patients (12%) had sinus rhythm restored, as compared with only 3 of 201 patients (1%) given placebo. Once sinus rhythm was restored, dofetilide was significantly more effective than placebo in maintaining sinus rhythm ($p < 0.001$). As a pure class III agent, it has no negative inotropic effects, even in patients with markedly impaired left ventricular function (31). Thus, dofetilide is a useful drug to consider in the management of the common combination of heart failure and atrial fibrillation. The risk of developing torsades de pointes is 3.3% (30).

Nonpharmacologic Therapy for Conversion and Maintenance of Sinus Rhythm

Pharmacologic treatment has been used for decades for cardioversion and prevention of recurrent atrial fibrillation but the use of antiarrhythmic drugs is associated with substantial side effects and proarrhythmia in some patients (Table 3). Accordingly, it is not surprising that nonpharmacologic techniques have been developed for the management of AF, including external and internal electrical cardioversion, atrial pacing methods to prevent AF, and several surgical or radiofrequency catheter ablation procedures. The current nonpharmacologic

TABLE 3
Side Effects of Current Antiarrhythmic Therapies in AF

Antiarrhythmic	Side Effects
Class Ia	Proarrhythmic and/or torsades de pointes
Quinidine	Diarrhea, hypotension, cinchonism, torsades de pointes (4.4%)
Procainamide	SLE (20%), hypotension, agranulocytosis
Disopyramide	Anticholinergic effects (29%), hypotension
Class Ic	Proarrhythmic
Flecainide	Significant negative inotrope, neutropenia, ventricular proarrhythmia (5–30%)
Propafenone	Nausea, dizziness, cholestatic jaundice, headache, ventricular proarrhythmia (5%)
Class III	Proarrhythmic and/or torsades de pointes
Amiodarone	Hyper-/hypothyroidism, pulmonary fibrosis, corneal deposits, blue-gray skin
Sotalol	Proarrhythmic Torsades de pointes (2.5%)
Ibutilide	Proarrhythmic Torsades de pointes (4.3%)
Dofetilide	Proarrhythmic Torsades de pointes (3.3%)

SLE = systemic lupus erythematosus

therapies and their mechanisms of action, as well as their potential limitations, are summarized in Table 4.

Atrial implantable defibrillator. Patients for whom external cardioversion is unsuccessful present a management dilemma and are often considered to have permanent AF. For this small but significant group of patients, internal cardioversion is thought to be of value. The rationale for internal cardiac defibrillation in this setting is to decrease the amount of extracardiac tissue involved in the current path, which maximizes the potential gradient within the atrial tissue and increases the success rate of atrial defibrillation. In recent years there has been a substantial effort to develop a catheter-based lead system for internal atrial defibrillation (32).

Low-energy internal atrial defibrillation has been performed in animals and humans (32). The lowest defibrillation threshold of available transcatheter techniques with an energy of 1.1 to 8.9 joules (J) was found in the region between the coronary sinus and the right atrium.

TABLE 4
Mechanisms and Limitations of the Current Nonpharmacologic Therapies for AF

Nonpharmacologic Method	Mechanism	Limitations
Atrial Defibrillator	Internal defibrillation (1.1–8.5 J)	Painful and intolerable
Atrial Pacing	Biatrial synchronous pacing	Sick sinus syndrome patients only
Palliative Catheter Ablation	Modification or ablation of the atrioventricular node	Requires permanent pacemaker implantation
Surgical Maze	Multiple linear atrial incisions	Prolonged cardiac ischemic time during procedure
Curative Catheter Ablation	Multiple linear atrial lesions by radiofrequency energy or focal lesions at the pulmonic veins	High recurrence and pulmonic vein stenosis

Low-energy transcatheter atrial defibrillation is safe, with few complications and high success rates. Some of the reported complications have been: subclavian venous thrombosis, pericardial effusion and lead dislodgement (33–35). Unfortunately, even with the low energies used, the shocks are often painful and intolerable to the patient (33). This reduces the clinical utility of the current implantable atrial defibrillator models.

Both single-chamber and dual-chamber defibrillating devices are available. The METRIX device or Atrioverter (InControl, Redmond, WA) (35), was the first implantable atrial defibrillator developed; it entered the clinical arena in 1995, weighing 82 g. This unit has sensing and defibrillation capability in the atrium and sensing and pacing capability in the ventricle. Its maximal output for atrial shocks is 6.4 J. In the METRIX clinical study of patients with AF (36), a total of 290 patients had the device implanted. Every patient had failed 4 antiarrhythmic drugs. Their average ejection fraction was 50%. In the clinical trial, a total of 614 episodes of AF were treated with 1,497 shocks, with 2.4 shocks per episode. There was a 93% conversion rate to sinus rhythm. In a more recent multicenter study, Wellens et al. (35) present their first experience with the Atrioverter. With 51 patients, the overall success rate of the device for cardioversion to stable sinus rhythm with or without additional drugs was 86%.

Another unit, the JEWEL AF 28 (36) (Medtronic, Minneapolis, MN), is a similar device, weighing 93 g and having dual-chamber sensing and pacing as well as defibrillation ca-

pability in both the atrium and ventricle. Its maximum output is 27 J. This unit has wide flexibility as a ventricular defibrillator capable of atrial defibrillation as well. It has been found to detect and treat atrial and ventricular arrhythmias appropriately. Termination of episodes of spontaneous atrial flutter and AF is achieved by pacing.

Although these devices are promising, the factor which limits their widespread use is not safety or efficacy, but patient comfort. Any defibrillating shock greater than 1 J is uncomfortable for most patients. Mean defibrillation threshold in the METRIX experience was approximately 3 J. The atrial defibrillator needs to err on the side of not giving inappropriate shocks for a nonlethal rhythm, in contrast to ventricular defibrillators, which must not miss lethal ventricular arrhythmias (32).

Atrial pacing. Cardiac pacing in atrial fibrillation has been prescribed in the past for patients with a slow ventricular response. Several studies suggest that atrial-based cardiac pacing may be beneficial in decreasing AF episodes. Two pacing modalities have been studied, anti-bradycardia and multi-site pacing.

Pacing to prevent atrial fibrillation in sick sinus syndrome. Patients with sick sinus syndrome commonly develop supraventricular tachycardias, predominantly atrial fibrillation (tachycardia-bradycardia syndrome). There has been much debate on whether atrial-based or ventricular-based pacing is preferred for sick sinus syndrome patients. Retrospective studies

have evaluated the incidence of atrial fibrillation in patients with single-chamber ventricular pacing versus atrial pacing or dual chamber pacing. Results indicated that the incidence of atrial fibrillation was reduced in patients who received atrial-based pacing (37). By inhibiting or triggering pacing in patients in whom VVI (ventricle paced, ventricle sensed and inhibited response to sensing) was used, the annual incidence of atrial fibrillation was 5–15% versus 1–3% in patients in whom either AAI (atria paced, atria sensed and inhibited response to sensing) or DDD (dual-chamber paced, dual-chamber sensed) was employed. Decreased incidence of stroke and congestive heart failure, with a trend to lower mortality was noted. This is probably due to restoration of synchronous contraction of the atria.

A randomized prospective study compared AAI to VVI pacing (38). The investigation included 225 consecutive patients with the sick sinus syndrome, randomized to atrial or ventricular pacing and followed for 5 years. The results show a trend to an increased incidence of atrial fibrillation and stroke in patients receiving VVI pacing. The incidence of atrial fibrillation was 14% in the AAI group and 23% in the VVI group ($p=0.12$). Thromboembolic events occurred in 17.4% of the VVI group but in only 5.5% of the AAI group ($p=0.0083$). There was no difference in mortality or development of congestive heart failure. In summary, the data support use of atrial-based pacing in patients with sick sinus syndrome.

Multisite pacing. Intra-atrial conduction block results in a very delayed activation of the left atrium, and may be associated with an increased incidence of atrial tachyarrhythmias. In a preliminary study of 28 patients, permanent atrial resynchronization resulting from simultaneous right atrial and coronary sinus pacing corrected the intra-atrial dyssynchrony expressed by reduction of P-wave duration (39). In 21 patients, this biatrial synchronous pacing prevented arrhythmia recurrences during follow-up of 34 ± 15 months (39). Use of dual-site atrial pacing, in the high right atrium and coronary sinus, was evaluated in a prospective study in fifteen patients with paroxysmal atrial fibrillation who had bradyarrhythmias warranting permanent pacemaker implantation (40). Dual-site atrial pacing with an optimal drug regimen resulted in a marked decline in atrial fibrillation recurrences. Multisite atrial pacing is feasible and safe, and appears to be effective.

Further research may demonstrate that this pacing modality should be considered as a primary mode of treatment to prevent AF.

Palliative catheter ablation. The palliative ablative procedures that are available for the treatment of atrial fibrillation are AV junctional ablation and AV nodal modification. The goal of AV junctional ablation is to interrupt completely the AV conduction with a lesion placed in the immediate area of the AV node. In most cases after AV junctional ablation, the patient has a slow but tolerable junctional escape rhythm originating from the low AV node or high His bundle region immediately distal to the site of ablation. This escape rhythm is usually adequate to prevent hemodynamic embarrassment, but not adequate to maintain a normal heart rate at rest or with activity. Therefore, permanent ventricular pacemaker implantation is always required.

AV junctional ablation and permanent pacing. In some patients with permanent atrial fibrillation, drug therapy to control ventricular response is either ineffective or not tolerated. An alternative approach is endocardial catheter ablation of the AV junction that results in complete heart block (41). These patients require a permanent pacemaker. Improvement in exercise tolerance (41) and quality of life (42) has been demonstrated with this procedure.

The technical success rate of AV junctional ablation is excellent, ranging from 95–100%, when performed by experienced operators (43). In appropriately selected patients, marked improvement in symptoms can be anticipated, with decreases in palpitations, effort dyspnea and exertional intolerance. Improvements in exercise time and ventricular function have been measured 3 months after ablation. In one study of patients with atrial fibrillation and reduced left ventricular function, 90% of patients had improvement in their left ventricular ejection fractions and a decrease in left ventricular and atrial dimensions (43). Another recent, large, multicenter trial, the Ablate and Pace Trial (APT) (44), treated 157 patients with ablation-paced therapy. In 14 of 46 patients, there was a dramatic increase in ejection fraction, from a mean ejection fraction of 33 to 61% at 3 months (41, 44). Cardiac output was not measured. Other studies have also seen significant improvements in ejection fraction from 43 to 54% post-ablation (45), as well as improvements in treadmill exercise performance (41).

AV node modification. Total AV junction ablation requires pacemaker implantation. Another technique for slowing the ventricular rate during AF without creating irreversible heart block has been developed. The method involves modifying AV node conduction to prevent rapid ventricular rates. Several studies have demonstrated the feasibility of modifying AV node function without creating AV block (46, 47). AV node modification is effective in about 70% of patients. Inadvertent AV block may occur in 16% to 21% of patients, and one episode of sudden death has been reported (46).

The goals of AV nodal modification procedures are to damage but not destroy all AV nodal conduction. In the ideal case, the patient will have adequate basal rates, but the rapid acceleration of the ventricular rate with exercise or stress will be prevented. It is important to note that the atria will continue to fibrillate after AV junctional ablation or modification, despite excellent heart-rate control and resolution of the patient's symptoms. Therefore, the patient is still at risk for stroke, and ongoing treatment with anticoagulation is recommended.

The acute success rate of AV nodal modification procedures is approximately 70% (48, 49). Because the injury to the AV node is non-specific, the frequency of complete heart block with this procedure ranges from 0–21% (48, 49). Clinical outcome has been favorable in patients with an initial successful response over short-term follow-up. Even with successful heart-rate control, patients treated with AV nodal modification will continue to have an irregular ventricular response to their atrial fibrillation and may have persisting symptomatic palpitations. For this reason, AV junctional ablation and pacemaker implantation is the procedure of choice in most cases.

Surgery. Several surgical approaches have been used to treat patients with AF (4, 50). The most popular is the MAZE (4) operation, where multiple atrial incisions are made to channel sinus impulses through a path, or "maze," to reach the AV node. This prevents a large area of contiguous atrial tissue from sustaining AF while maintaining atrial contractility. The long-term effects of this technique have been favorable and effective (4). In a study of 178 patients, 32 patients underwent the Maze-I procedure, 15 underwent the Maze-II procedure, and 118 underwent the Maze-III procedure. During the follow-up (3 months to 8 years), patients were accessed for recurrence of atrial

flutter and atrial fibrillation. Ninety-three percent (93%) of the patients were arrhythmia free. Another study by Kosakai et al. (50), had a success rate of 84% with a modified MAZE procedure.

The most successful is the Maze III procedure (43). It is a complex operation, which involves a number of predesignated incisions in both atria, along with cryolesions applied at certain points. The objective is to interrupt micro re-entrant circuits in the atria while ensuring that the SA node is able to generate and propagate the sinus impulse through both atria. This procedure requires prolonged myocardial ischemia and cardiopulmonary bypass, which detracts from its utility despite its success. Results from surgical approaches suggest that large areas of the atria must be isolated electrically to prevent AF. Efforts are underway to replicate the MAZE incisions using radiofrequency energy to produce equally effective intramural ablation more quickly and with less risk. Catheters capable of creating contiguous, multiple, transmural, linear lesions also are being developed to facilitate rapid ablation of AF of the atria. Their introduction will significantly shorten the duration of the MAZE procedure (43).

Early results have been promising, but long-term follow-up of substantial numbers of patients with a variety of causes of AF is lacking. Many patients may require implantation of a permanent pacemaker after the MAZE procedure.

Curative catheter ablation. The MAZE procedure has been the primary surgical treatment for atrial fibrillation (4). A procedure in which linear lesions create endocardial compartmentalization and a maze-like result has been developed using radiofrequency catheter ablation energy (5).

Since the size of the reentrant circuit is determined by the conduction velocity and refractoriness of the tissue (51), the imposition of conduction blocks at critical anatomical sites may inhibit the propagation of the fibrillatory waves. This was the theoretical basis of the MAZE procedure (52). It was hypothesized that similar, long, linear atrial lesions could be achieved by catheter ablation.

Experimental studies have demonstrated that multiple linear lesions in the right and left atria can prolong atrial fibrillation cycle length and, ultimately, terminate this ongoing arrhythmia. It was also demonstrated that lesion continuity was not necessary for successful termination and prevention of reinitiation of the

atrial fibrillation (52). The first cases of atrial fibrillation ablation in patients employed a technique of dragging a typical 4 mm tip ablation electrode along the atrial wall during ongoing radiofrequency energy delivery. Chronic atrial fibrillation could be successfully terminated in the majority of cases, but over half of the patients had arrhythmia recurrence and required at least a second ablation session (43).

In a study of 224 patients (5) with paroxysmal AF, 45 patients received a linear right-atrial ablation, 44 patients received right-atrial, septal, and left-atrial ablations and 135 patients received a focal ablation in the pulmonary veins. The catheter was introduced into the left atrium transseptally. The right atrial ablation cure rate was 15% and the combined bi-atrial cure rate was 57%. The pulmonary vein experience is by far the most interesting. The success rate varied between 20% (if only 4 pulmonary veins were involved) and 89% (if 1 pulmonary vein was involved). The overall success rate was 69% (5). Right atrial catheter ablation failed to terminate atrial fibrillation. In contrast, left atrial ablation, either alone or after right atrial ablation, was found to be highly effective in the termination of chronic atrial fibrillation (in 28 of 30 patients, sinus rhythm was restored) (5). In addition, pulmonary vein ablation has shown promising results in the termination of paroxysmal AF (5, 6).

A new approach to catheter ablation of atrial fibrillation. A new approach to catheter ablation of AF is now under investigation and is claimed to have an advantage over the radiofrequency techniques currently used. This catheter technique uses ultrasound energy in a through-the-balloon procedure developed at and licensed to Atrionix (Palo Alto, CA), and is already in clinical trials in both the U.S. and Europe (53).

Ultrasound through a balloon. This new approach to ablation of AF focuses on the pulmonary veins and uses sound waves to destroy errant heart tissue. This method, also known as anatomic pulmonary vein isolation with through-the-balloon ultrasound ablation (TTB-USA) (53), was invented by Lesh. It is based on the principle that a circumferential lesion at the base of one or more pulmonary veins would electrically isolate the veins from the atrium. Therefore, the electrical activity from within those veins would be unable to reach the body of the atrium and thus could not trigger or potentiate AF.

To perform the circumferential lesion, Lesh and colleagues developed a novel over-the-wire catheter design that integrates a cylindrical ultrasound transducer within a saline-filled balloon, which is introduced transseptally. The balloon is placed at the mouth of one or more of the pulmonary veins, allowing ultrasound ablation of a narrow ring of tissue in the area where the vein meets the atrium (53).

Summary

The three therapeutic goals that should be considered for every patient with AF are: (a) rate control, (b) maintenance of sinus rhythm, and (c) prevention of thromboembolism. It is unclear at this moment whether a strategy of primarily rate control or maintenance of sinus rhythm is superior.

The limited efficacy and proarrhythmic risks of antiarrhythmic drug therapies for atrial fibrillation have led to the development of nonpharmacologic therapeutic approaches. The interventional therapies that are currently being examined include prophylactic atrial pacing, atrial defibrillator therapy, atrial surgery, and catheter ablation of atrial fibrillation. All of these strategies, including the MAZE surgical procedure, are directed either at prevention or termination of atrial fibrillation, whereas the presently established nonpharmacologic options of atrioventricular (AV) nodal ablation followed by pacemaker implantation or AV nodal modification only offer ventricular rate control.

Conclusion

When planning treatment for AF, different pharmacologic therapies should be considered along with nonpharmacologic strategies. Pathophysiology of AF is probably multi-factorial, i.e., ectopic focus (pulmonary veins) and reentry (the atria). Evaluating the factors involved in any patient with acute or recurrent paroxysmal AF, or chronic AF, may enhance the success of the options: using various drugs alone, nonpharmacologic procedures, or a combination of both.

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