Nonpharmacological Approaches to Atrial Fibrillation
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The mainstay of managing atrial fibrillation (AF) is drug therapy. In some patients, drug therapy is ineffective or not tolerated. This article reviews the current status of various nonpharmacological options for the treatment of AF.

Atrioventricular Junction Ablation
Transvenous ablation of the atrioventricular (AV) junction was first performed with direct-current shocks in 1981. 1 Radiofrequency energy replaced direct-current shocks for AV junction ablation because of improved efficacy and safety. 2 Radiofrequency ablation of the AV junction has a success rate >95% and is associated with a low incidence of adverse effects. 3 Although sudden death due to ventricular tachycardia/fibrillation may occur after successful ablation of the AV junction, 3 this risk may be minimized by pacing at a lower rate limit of 80 to 90 beats/min for several days to weeks after ablation.

Long-Term Observations
Retrospective studies have documented long-term improvement in quality-of-life, functional capacity, and left ventricular function in patients with impaired systolic function who undergo AV junction ablation. A prospective study confirmed an improvement in both quality-of-life and ventricular function in these patients, and it also demonstrated a reduction in long-term costs compared with standard drug therapy. 4 These findings are supported by a recent meta-analysis, which also found no evidence of a higher mortality rate in patients who had undergone AV junction ablation than in those in large anticoagulant trials. 5

Summary
The available data indicate that AV junction ablation improves quality-of-life, functional capacity, and ventricular function. Compared with other types of nonpharmacological therapy for AF, a major advantage of AV junction ablation is that its success rate approaches 100%. However, the disadvantages of AV junction ablation include the lifelong need for a pacemaker and an ongoing risk of thromboembolic complications.

AV junction ablation is appropriate in symptomatic patients with AF and an uncontrolled ventricular rate who have failed treatment with several antiarrhythmic drugs (often including amiodarone), particularly when there is evidence of a tachycardia-induced cardiomyopathy. Because of lifelong pacemaker dependency, an alternative form of nonpharmacological therapy may be more suitable for the younger patient with drug-refractory AF.

AV Node Modification
Several studies have demonstrated that radiofrequency energy applied to the right posterior or midseptal regions results in a significant and sustained reduction in ventricular rate during AF in 60% to 85% of patients. 6–8 In one study, this procedure was associated with a 21% incidence of either early or late AV block. 6 Compared with AV junction ablation, the advantage of AV node modification is the achievement of rate control during AF without the need for long-term pacing. However, AV node modification has not achieved widespread use because of a high recurrence rate and because symptoms caused by an irregular rhythm may persist. An attempt at AV node modification is most appropriate in patients who are appropriate candidates for AV junction ablation and who wish to avoid pacemaker implantation. Because of a high risk of AV block, AV node modification should not be recommended in patients who consider the possibility of pacemaker implantation unacceptable.

Atrial Pacing to Prevent AF
Vagotonic AF
Coumel et al 9 demonstrated the efficacy of atrial pacing in patients with AF of vagal origin. These patients have AF triggered by sinus bradycardia or atrial bigeminy, usually at rest, during sleep, or after meals. Typically, vagotonic AF is paroxysmal and occurs in men without the sick sinus syndrome or structural heart disease. If treatment with a vagolytic antiarrhythmic drug such as disopyramide is ineffective, atrial pacing may be appropriate.

Pacing in Patients With the Sick Sinus Syndrome
Retrospective studies have shown that atrial-based pacing in patients with the sick sinus syndrome is superior to ventricular demand pacing with respect to the incidence of AF and the risk of cerebrovascular accidents, congestive heart failure, and overall mortality. This has been confirmed in prospective, randomized trials. 10,11 However, when bradycardia is not
an indication for pacing, atrial-based pacing may not prevent episodes of AF.\textsuperscript{12}

**Dual-Site Atrial Pacing**

Dual-site atrial pacing results in more homogeneous atrial depolarization and repolarization than conventional pacing, and it is more efficacious than single-site pacing for preventing AF.\textsuperscript{13,14} However, it is important to note that the patients in these studies had a bradycardia indication for pacing, and they continued to require treatment with antiarrhythmic drugs.

**Summary**

The bulk of available data supports the use of atrial-based pacing for the purpose of decreasing the incidence of AF episodes in patients with vagotonic AF or sinus node disease. Atrial pacing cannot be justified on the basis of existing data in patients with nonvagotonic AF or those without sinus node disease. Although dual-site atrial pacing remains an intriguing and potentially important treatment modality, its efficacy requires confirmation in prospective, randomized trials.

Patients should be informed that antiarrhythmic drug therapy often continues to be required after pacemaker implantation. If AF remains troublesome despite pacing, AV junction ablation can be considered as a next step in management.

**Internal Atrial Defibrillator**

By preventing remodeling, rapid conversion of AF may decrease the predisposition toward additional episodes of AF. An implantable atrial defibrillator in theory is an excellent modality for the detection and rapid conversion of AF. Implanted atrial defibrillators are safe and have an 80% efficacy in terminating AF.\textsuperscript{15} Limited data suggest that early cardioversion by the implanted atrial defibrillator prolongs the interval between recurrent episodes of AF.\textsuperscript{16} The drawbacks of the implanted atrial defibrillator include discomfort from the shocks, early recurrence of AF, and technical problems with the device.

Because frequent shocks are undesirable, the ideal candidate for an implanted atrial defibrillator has infrequent episodes of symptomatic, drug-refractory AF. However, if episodes of AF are rare, it is difficult to justify implanting a device. At present, the implanted atrial defibrillator is available only in combination with a ventricular defibrillator.

**Surgical Treatment of AF**

**Maze Procedure**

Creating anatomic barriers in the atria may decrease the number of circulating wavelets to a level below the critical number required to sustain AF. Accordingly, Cox et al\textsuperscript{17} demonstrated that a series of atrial incisions in patients with AF was often effective in restoring and maintaining sinus rhythm long-term. This “maze” procedure has been refined, and it is typically performed in association with mitral valve or coronary bypass surgery. In recent studies of 39 to 100 patients undergoing the maze procedure, 74% to 90% of patients were in sinus rhythm at 2 to 3 years postoperatively.\textsuperscript{18,19} The operative mortality rate is ≤1%, but up to 6% of patients have required a pacemaker.\textsuperscript{18,19} In >90% of patients, the right and left atria regain mechanical function.\textsuperscript{20} The maze procedure has also been performed in patients with lone paroxysmal AF, with a 95% success rate.\textsuperscript{21}

**Other Surgical Approaches**

Another intraoperative approach for treating AF in patients undergoing valve surgery has consisted of cryoablation limited to the posterior left atrium. Linear cryolesions connecting the 4 pulmonary veins and the posterior mitral annulus were effective in restoring sinus rhythm long-term in 69% of patients with chronic AF.\textsuperscript{22}

At the time of mitral valve repair or replacement, endocardial isolation of the pulmonary veins was performed under direct visualization using an electrode catheter in 43 patients with chronic AF and dilated atria.\textsuperscript{23} At 1 year postoperatively, 30% of patients were in sinus rhythm and had functioning atria. Although this is a low success rate, the study demonstrates that the pulmonary veins may sometimes play a critical role in maintaining AF, even in patients with mitral valve disease and a dilated left atrium. In such patients, chronic atrial remodeling might have been expected to make AF permanent, independent of the pulmonary veins.

**Summary**

Surgical therapy for AF is most appropriate in patients who require open-heart surgery for another indication. In such patients, AF is often eliminated with little or no increase in morbidity or mortality. In patients with lone AF or no other indication for surgery, an intraoperative approach for the treatment of AF may be unattractive because of the potential risks, discomfort, and prolonged convalescence associated with heart surgery.

**Focal Catheter Ablation of AF**

**Background**

There are 2 different types of arrhythmias that may play a role in generating AF, and both may be addressed by focal ablation. One type of arrhythmia is a premature depolarization that initiates AF.\textsuperscript{24} A second type is a focal tachycardia that either induces fibrillation in the atria or mimics AF by creating a pattern of rapid and irregular depolarization wavefronts in the atria.\textsuperscript{25} Focal tachycardias that initiate or mimic AF can be recognized in the electrophysiology laboratory because they are frequently associated with exit block between the site of origin of the tachycardia and the rest of the atria.\textsuperscript{26}

Although focal sources of AF may be found in the right atrium, left atrium, coronary sinus, superior vena cava, or vein of Marshall, 95% of foci are located within a pulmonary vein.\textsuperscript{27} The pulmonary veins are covered by myocardial sleeves formed by one or more layers of myocardial fibers oriented in circular, longitudinal, oblique, or spiral directions.\textsuperscript{28} These sleeves vary from 2 to 25 mm in length, with a mean length of \(\approx 10\) to 20 mm in the superior pulmonary veins and 5 to 10 mm in the inferior pulmonary veins.\textsuperscript{28,29} The difference in the length of the sleeves may explain why arrhythmogenic foci are found more often in the superior than in the inferior pulmonary veins. The arrhythmogenic nature of these myocardial sleeves may be due in part to their
embryonic origin from the same substrate that gives rise to the conduction system, which may be subject to abnormal automaticity. However, it is unclear whether the arrhythmias that arise in pulmonary veins are most often due to automaticity, reentry, or triggered activity, and it is possible that more than one mechanism plays a role in generating these arrhythmias.

**Focal Ablation Within Pulmonary Veins**

One approach to the ablation of a pulmonary vein arrhythmia that triggers or simulates AF is to target the site of origin of the arrhythmia within the pulmonary vein directly. Localization of the site of origin of the arrhythmia is guided by the endocardial activation time. Two published studies have described the results of focal ablation within a pulmonary vein with ≥6 months of follow-up. These studies consisted of 41 to 79 patients who had frequent atrial ectopy and episodes of paroxysmal AF, and 65 to 103 ectopic foci originated within a pulmonary vein. Radiofrequency ablation was guided by activation mapping, and a mean of ≈4 to 7 applications of radiofrequency energy was delivered in the pulmonary veins. In one of the studies, ≈75% of patients required a second or third ablation procedure, and after a mean follow-up interval of 8 months, 62% of patients were free of symptomatic AF in the absence of antiarrhythmic drug therapy. The results were more impressive in the other study, with only 7% of patients needing a second ablation procedure and a success rate of 86% at a mean of 6 months of follow-up. However, in a later publication from the same laboratory, the recurrence rate at a mean of 8 months of follow-up had increased to 25%.

The most common complications associated with the focal ablation of arrhythmias arising within the pulmonary veins are pericardial effusion (≤4%), transient ischemic episodes (≤2%), and symptomatic pulmonary vein stenosis (≤2%). Although asymptomatic pulmonary vein stenosis may occur as many as 40% of sites at which focal ablation is performed, the risk of symptomatic pulmonary vein stenosis seems to be small if the number of radiofrequency applications delivered within pulmonary veins is kept to a minimum.

The early experience with the focal ablation of pulmonary vein arrhythmias indicates that the recurrence rate is high and the success rate only modest, even in experienced laboratories. The suboptimal results can be attributed to the limitations of the technique, which include the following: (1) many patients have multiple foci; (2) there may be a paucity of spontaneous or inducible arrhythmias during the procedure; (3) new foci may emerge after the procedure; (4) the risk of pulmonary vein stenosis limits the amount of radiofrequency energy that can be safely delivered within a pulmonary vein; and (5) mapping may be made difficult by frequent recurrences of persistent AF.

**Pulmonary Vein Isolation**

The limitations associated with focal ablation within pulmonary veins have prompted the development of other techniques for eliminating the pulmonary vein arrhythmias that trigger or mimic AF. One alternative is electrically isolating the pulmonary veins by circumferential ablation at their ostia. An anatomically based procedure eliminates the need for spontaneous or induced arrhythmias, eliminates the need for mapping, and would be effective in preventing recurrent AF caused by multiple pulmonary vein foci, even if new foci emerge at some future time.

Two techniques have been used to isolate pulmonary veins electrically. One technique involves the delivery of multiple, contiguous point applications of radiofrequency energy in a circumferential fashion in the left atrium near the ostia of the pulmonary veins. Another technique uses ultrasound energy to create a circumferential lesion with a catheter that has an ultrasound transducer mounted near its tip. The transducer is inside an inflatable balloon that is used to occlude the pulmonary vein and to stabilize the transducer at the left atrial–pulmonary vein junction. This technique was successful in 67% of 15 patients with paroxysmal or persistent AF.

In theory, anatomically based techniques for pulmonary vein isolation have significant advantages over focal ablation within the pulmonary veins. However, the published experience with these techniques is minimal, and their feasibility and safety remain to be established.

**Segmental Isolation of Pulmonary Veins**

The myocardial fibers that envelope the pulmonary veins may not be present along the entire circumference of the pulmonary vein ostia. Therefore, to eliminate conduction in and out of a pulmonary vein, ablation along the entire circumference of the ostium may not be necessary. Instead, radiofrequency energy can be targeted to the segments of the ostium at which muscle fibers are present. These sites are identified by the presence of high-frequency depolarizations, which likely represent pulmonary vein muscle potentials. The recording of ostial pulmonary vein potentials is facilitated by catheters that have multiple electrodes along a distal loop that fits within the ostium. There is compelling evidence that electrical pulmonary vein isolation can be achieved by selective ablation of ostial sites where a pulmonary vein potential is recorded, which may encompass as little as 25% of the circumference of the ostium. In the experience of the authors, complete electrical isolation may be achieved with as few as 1 to 5 applications of radiofrequency energy.

Because ostial pulmonary vein potentials can be recorded during sinus rhythm or atrial pacing, a segmental approach to pulmonary vein isolation does not require detailed mapping of spontaneous ectopy. It is sufficient to identify which veins are arrhythmogenic, which is usually a much simpler task than pinpointing the site of origin of a focus within a pulmonary vein. If no ectopy is present during the ablation procedure, it may be appropriate to perform empiric segmental isolation of the left and right superior and left inferior pulmonary veins, because these are the most common sources of the arrhythmias that trigger AF.

Another advantage of this technique is that the end point of ablation is unambiguous. The elimination of all pulmonary vein potentials within the pulmonary vein indicates that there are no remaining muscle fibers at the ostium that are capable of conducting impulses in or out of the pulmonary veins. In one study of 90 patients with paroxysmal AF, the success rate
in preventing recurrent AF in the absence of drug therapy at a mean of 8 months of follow-up was 90% when pulmonary vein potentials were eliminated in all arrhythmogenic pulmonary veins, compared with only 55% when pulmonary vein potentials were still present in ≥1 pulmonary veins.36

In that study, no instances of pulmonary vein stenosis occurred when the power of radiofrequency applications was limited to 30 W, even when ostial ablation was circumferential.36

The initial experience with segmental ostial ablation of pulmonary veins guided by pulmonary vein potentials is encouraging, with a long-term success rate of 90% in patients with paroxysmal AF and with minimal or no risk of pulmonary vein stenosis when the power of radiofrequency energy applications is limited to 30 W. Major advantages of this technique are that it eliminates the need for detailed mapping of all pulmonary vein foci and that there is a clear-cut end point of ablation, even when spontaneous arrhythmias are absent. Furthermore, the procedure can be performed with conventional ablation catheters and does not require specialized tools such as a balloon ultrasound ablation catheter. However, occasional patients may remain symptomatic from AF triggered by ectopy arising at sites other than the pulmonary veins.

Chronic AF
Little data are available as yet regarding the efficacy of radiofrequency ablation within pulmonary veins in the electrophysiology laboratory in patients with chronic AF. In 2 studies, an arrhythmogenic pulmonary vein was identified in a total of 18 patients with chronic AF by mapping the ectopy that resulted in early recurrence of AF after repeated trans-thoracic or transvenous defibrillation.37,38 Radiofrequency ablation, either at the pulmonary vein ostia or within the pulmonary veins, resulted in long-term sinus rhythm in 60% to 67% of patients.

The early experience with focal ablation in patients with chronic AF is not sufficient to justify its widespread clinical application. The proportion of patients with chronic AF in whom a focal reinitiating trigger can be identified and the long-term outcome after the radiofrequency ablation of these triggers remain to be determined. Also unclear at this time is whether chronic AF is more amenable to a focal approach directed at the pulmonary veins or to linear ablation in the atria.

Summary
At present, the best candidates for the elimination of focal triggers of AF are symptomatic, drug-refractory patients with paroxysmal AF and normal or only mildly enlarged left atria. On the basis of the limited data available to date, the most appropriate ablation strategy that is currently feasible in clinical practice may be to identify the pulmonary vein or veins that are arrhythmogenic and to attempt to isolate these veins with segmental ostial lesions guided by pulmonary vein potentials aimed at eliminating all conduction pathways in and out of the veins.

Linear Catheter Ablation of AF

Background
Attempts to replicate the results of the maze procedure in the electrophysiology laboratory have consisted of the creation of linear lesions in the left and/or right atria. The linear lesions have been produced either with individual, contiguous applications of radiofrequency energy on a point-by-point basis or with multiple catheters with coil electrodes that are positioned against the atrial wall and that produce a linear lesion without having to repeatedly reposition the catheter.

Right Atrial Ablation
In some studies, linear ablation for AF has been confined to the right atrium. Although AF is probably never an exclusively right atrial arrhythmia, by eliminating the circulating wavelets in the right atrium, linear ablation confined to the right atrium may be helpful by either promoting early conversion of AF or improving the response to drug therapy. The number of linear lesions created in the right atrium most commonly has been 3, with a range of 1 to 4.39–43 The most common locations of the ablation lines are between the inferior and superior vena cava; the septum; and the cavotricuspid isthmus.

In 5 studies, 8 to 45 patients underwent linear ablation in only the right atrium.39–43 In most patients in these studies, AF was idiopathic and paroxysmal. During mean follow-up intervals of 6 to 21 months, only 6% to 25% of patients remained free of symptomatic AF in the absence of antiarrhythmic drug therapy. An additional 20% to 58% of patients had a marked improvement in AF-related symptoms during treatment with antiarrhythmic medications that had been ineffective before the ablation procedure. Therefore, although linear ablation confined to the right atrium eliminates AF in only a small percentage of patients, it more often may be helpful in a palliative fashion by improving the response to drug therapy.

Left Atrial Ablation
Studies of linear left atrial ablation (with or without right atrial ablation) have included 10 to 19 patients followed for a mean of 6 to 11 months.39,41,43 The ablation technique has been either to encircle all 4 pulmonary vein ostia and connect this encircling lesion with the mitral annulus or to create linear lesions from the superior pulmonary veins through the ostia of the inferior pulmonary veins to the mitral annulus and between the 2 superior pulmonary veins. In 2 studies, 40% to 58% of patients had no recurrences of AF in the absence of antiarrhythmic drug therapy, and another 10% to 20% had an improvement during treatment with previously ineffective drugs.39,41 However, these results have not been reproducible, and in a third study, none of the 12 patients who underwent a combined right and left atrial approach had a successful outcome.43

Complications
Because there have been only a small number of clinical studies describing the results of linear ablation of AF and because these studies have included small numbers of patients and have used different techniques, a reliable estimate
of the magnitude of risk associated with linear ablation is not yet available. The most common complication that has been reported to occur as a result of linear ablation of AF in the left and/or right atria has been pericardial effusion, which occurred ≤11% of patients.\textsuperscript{39–43} A complication limited to linear ablation in the right atrium has been sinus node dysfunction, which has occurred in ≤8% of patients.\textsuperscript{39–43} Two serious types of complications limited to left atrial ablation are cerebral infarction, which has been reported in ≤8% of patients,\textsuperscript{39,41–43} and pulmonary vein stenosis, the incidence of which is unclear. An anecdotal report documented the occurrence of pulmonary vein stenosis causing symptomatic pulmonary hypertension in 2 patients who underwent linear ablation in the left atrium,\textsuperscript{44} but this complication was not observed in any of the published series of patients who underwent linear ablation of AF.

Limitations of Linear Ablation of AF

Conduction block across a linear radiofrequency lesion in the atrium usually requires continuous transmural necrosis. In the electrophysiology laboratory, continuous lesions that result in complete conduction block are difficult to achieve, particularly in the left atrium and when using individual, contiguous applications of radiofrequency energy with a conventional ablation catheter. Precise manipulation and stabilization of an electrode catheter in the left atrium is a technically challenging and lengthy process, even in the hands of experienced operators using specialized guiding sheaths and sophisticated mapping systems that allow tagging of ablation sites. In a study in which an electroanatomic mapping system was used to guide the creation of linear ablation lines in the left atrium, the mean procedure duration exceeded 7 hours, and yet a set of ablation lines associated with complete conduction block could not be achieved in any of the 13 patients in the study.\textsuperscript{43}

Even when linear radiofrequency lesions are created under optimal conditions with a hand-held probe in the operating room, the ablation lines may often be discontinuous. An ablation line that creates incomplete conduction block may be sufficient to prevent AF, but it may be proarrhythmic, allowing new atrial reentrant tachycardias to emerge. Among 25 patients in whom linear, endocardial radiofrequency lesions were created under direct visualization in the left and right atria during open heart surgery, AF was successfully eliminated in 91% of patients.\textsuperscript{45} However, 6 of the 25 patients (24%) had postoperative atrial flutter that was attributable to reentry through a gap in an ablation line. The frequent failure to achieve complete conduction block, even when radiofrequency lesions are created under direct visualization in the open heart, emphasizes the tremendous challenge associated with creating complete lines of block in the electrophysiology laboratory.

Summary

The risk-benefit ratio of linear ablation in the left and/or right atrium remains to be defined. At present, this technique should be viewed as an investigational procedure and should be restricted to patients with symptomatic AF who have been refractory to multiple antiarrhythmic drugs.

Conclusions

In the minority of patients in whom AF cannot be adequately managed by pharmacological therapy, the most appropriate type of nonpharmacological therapy must be selected on an individualized basis. For example, in a cardiomyopathy patient with chronic AF and an uncontrolled ventricular rate, AV junction ablation may be the optimal therapy. In a patient with the sick sinus syndrome, atrial-based pacing (perhaps biatrial) may be the most appropriate option. In a patient who requires an implantable cardioverter-defibrillator and who has occasional episodes of AF, implantation of a device capable of both atrial and ventricular defibrillation should be considered.

If the patient has idiopathic AF, an attempt at curative therapy is often the most attractive option. In the opinion of the authors, the best technique currently available for curing paroxysmal AF (assuming it originates from the pulmonary veins) is segmental isolation of the pulmonary veins by discrete applications of radiofrequency energy at the ostia, guided by pulmonary vein potentials. Other techniques for pulmonary vein isolation, such as a balloon catheter used to create a circumferential lesion at the ostium, hold promise but require further development.

In the patient with idiopathic AF that is persistent or chronic, the best curative catheter ablation technique remains to be determined. On the basis of surgical experience and preliminary results with catheter techniques, it may be that the most effective curative catheter technique for chronic AF will be found to be pulmonary vein isolation in combination with linear ablation in the right and/or left atria. In the occasional patient who is disabled by chronic AF, referral for surgical treatment may be appropriate. However, at present, the most appropriate option for most patients with idiopathic chronic AF may be the use of pharmacological therapy to minimize symptoms as much as possible, prevent tachycardia-induced cardiomyopathy, and avoid thromboembolic complications, awaiting further improvements in curative catheter techniques.

References


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