Atrial fibrillation (AF) is one of the most challenging arrhythmias to treat. Many patients have to accept this disorder and the medications required. Nonpharmacologic therapies have emerged as alternative methods of treatment. However, technical difficulty, low success rate, high recurrence, and complications still are obstacles. Pulmonary veins as the most common trigger foci of paroxysmal AF are now the most interesting source of curative ablation. With more knowledge, technologies, techniques, and equipment, AF ablation is likely to be more successful. This article introduces some exciting aspects of pulmonary vein ablation, including our hope to cure AF in some selected patients. (Heart Lung® 2002; 31:271-8.)

Atrial fibrillation (AF) is the most common sustained cardiac rhythm disturbance and is associated with an increased risk of stroke, heart failure, and mortality.1-3 Its overall prevalence is 0.4% to 0.9%. Its incidence increases with age by about 0.1% to 0.2% per year after age 40, resulting in a prevalence of 2% to 4% in the population older than 60 years4-5 and 8.8% for those in their 80s. The important risk factors for the development of AF are rheumatic and ischemic heart disease, hypertension, and congestive heart failure. AF has a prevalence as high as 40% in patients with overt congestive heart failure.6 However, in 3% to 31% of documented cases of AF, no underlying cardiovascular disease can be detected (lone AF).4,7-10

Medications have been established as first-line therapy in patients with AF. However, many patients have drug-resistance or drug-intolerance. Dissatisfaction with pharmacologic therapy has resulted in a growing interest in nonpharmacologic treatments for AF. These aim to preserve or restore sinus rhythm and include bundle of His ablation and pacing, atrial pacing (single or multisite), implantable atrial defibrillator, catheter ablation, and surgery. Catheter techniques for ventricular rate control (atrioventricular junction ablation or modification) have been shown to be effective.11-13 If the procedure is performed by an experienced health care provider, the success of reducing complete AV block is more than 95%. The clinical efficacy in controlling arrhythmic symptoms and improving quality of life is well recognized in patients with paroxysmal AF but not yet in those with persistent or permanent AF. Moreover, there have been few data supporting the long-term effects of this therapy on cardiac performance, morbidity, and survival. In addition, the persistence of AF and the requirement for a permanent pacemaker have been significant drawbacks; the risks of thromboembolism and compromised hemodynamics remain.

Curative therapy of AF was developed by surgeons and then by electrophysiologists and consists of either approaching the substrate that maintains AF with linear lesions14-19 or eliminating the initiating triggers,20-24 especially in the pulmonary veins (PVs); the latter tends to be the current treatment of choice.

LINEAR ABLATION OF AF

Because of the hypothesis that AF is caused by multiple simultaneous wavelets of re-entry in the atria, complex surgical atriotomies and atriectomies have been performed with great success in curing AF.25-29 Catheter techniques were developed to compartmentalize the arrhythmia but had inconsistent results.30-36 In 1994, catheter ablation of AF in human beings was reported. Lesions restricted to the right atrium have been performed with success in treating patients with paroxysmal AF; however, in patients with chronic AF, a catheter-induced biastral
maze procedure was necessary.\textsuperscript{37,38} In these cases, creation of continuous linear transmural atrial lesions is necessary to prevent postprocedural macroreentrant atrial arrhythmias.

Usually, right atrial ablation is easy to perform, relatively safe, and has a low risk of thromboembolic stroke. However, there are some major risks due to cardiac conduction abnormalities and rightsided phrenic nerve paralysis. Several experimental and clinical observations demonstrated that right atrial ablation alone does not terminate AF in most patients,\textsuperscript{39,40} whereas left atrial linear lesions significantly increase the success rate.\textsuperscript{22,40} Roithinger et al\textsuperscript{41} showed that the left atrium is the driver during chronic AF. Therefore, the creation of extensive linear endocardial lesions in the left atrium is important.\textsuperscript{42} Results of clinical trials have shown that concern about left atrial endocardial ablation is well justified and that meticulous attention to anticoagulant therapy and temperature control are necessary to minimize the possibility of atrial charring, thrombus formation, and systemic emboli.

Left atrial linear ablation has been performed through the transeptal approach. These linear ablation procedures in the left atrium are time-consuming (mean, 10 hours) and associated with significant morbidity, notably pericardial effusion and thromboembolic events.

During earlier experience with linear ablation, it was thought that the left atrium may be the major driver in the mechanism of AF. Because of technical difficulty, current technology, and equipment delicacy, this procedure is not often performed. Complete ablation lines are difficult to perform in this chamber, and new catheter technologies are required to achieve compartmentalized lesions to prevent proarrhythmic discontinuities and arrhythmic recurrences. Because of these difficulties, current practice is directed at ablation of the initiating trigger foci (Table 1).\textsuperscript{43}

### Electrocardiographic study of PVs

Nearly 100% of cases of paroxysmal AF with or without ectopy or structural heart disease have focal triggers that can be ablated. These foci predominantly originate in the PVs with unusual characteristics, including long conduction time to the left atrium, unpredictable firing, and frequent occurrence of focal discharges confined within the vein. Rarely, triggers initiate from other veins (eg, superior vena cava, ligament of Marshall, coronary sinus) or atrial tissue, particularly in the posterior left atrium.\textsuperscript{20,44-50} Jais et al\textsuperscript{21} first described the focal source of AF in human beings and suggested that most spontaneous AF originates from PVs by abnormal automaticity or triggered mechanism.

During sinus rhythm, PV potentials—characterized by a sharp upstroke, narrow duration of less than 50 ms, and an amplitude of more than 0.05 mV—are usually preceded by a far-field atrial potential with a slow slope (depolarization rate \(dV/dT\) of less than 0.5 mV/s).

<table>
<thead>
<tr>
<th>Table I</th>
<th>Risk/benefit analysis of curative approaches for atrial fibrillation\textsuperscript{43}</th>
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<tr>
<td>Approach</td>
<td>Advantages</td>
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<tr>
<td>Trigger ablation</td>
<td>● Accessible with conventional catheters</td>
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<td></td>
<td>● No proarrhythmic effect of ablation</td>
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<td>Linear ablation in the LA</td>
<td>● Anatomic approach (no prior mapping required)</td>
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\(LA\), left atrium; \(PV\), pulmonary vein.
an apparently random “fibrillation” pattern of left atrial activation, which is much more suggestive of wandering re-entry. Initiation of common atrial flutter and its degeneration into AF or its interruption are also frequently caused by PV discharges. The first ectopic P wave, whether isolated or initiating AF, is superimposed on the T wave of the previous QRS complex, producing a P-on-T pattern that is recognizable at first sight. During an ablation procedure, any focus resulting in a P-on-T wave is considered to be a target for ablation, even when there is no documentation of its role in AF initiation. The reason for this is that when these foci were spared, most patients subsequently developed AF recurrences that originated from the unablated focus, which necessitated a second ablation procedure.

Arrhythmogenic PVs

Haissaguerre et al defined an arrhythmogenic PV as a PV (extending from the ostium to its tributaries) that gives rise to spontaneous discharges, single or multiple and with or without conduction to the left atrium.

During sinus rhythm, double or multiple potentials are recorded in sequence from the proximal to the distal PV, synchronous with the first (right-sided PVs) or second (left-sided PVs) half of the P wave. The first low-frequency potential reflected activation of the adjacent atrium. The last high-frequency potential indicated PV muscle potentials.

During ectopy from an arrhythmogenic PV, the activation sequence is reversed, from the distal to the proximal, with the PV potential preceding the left atrial potential. The conduction time to the left atrium is typically long and exhibits decremental conduction with increasing prematurity.

Candidates for PV ablation

In earlier reports, patients were selected for PV ablation on the basis of occurrence of frequent ectopy, which allowed mapping. The selection is now neither made on the basis of ectopy frequency nor structural heart disease. There are no definite criteria for identifying or excluding candidates for AF ablation. However, because of the current technical difficulties, patients with multidrug-resistant AF are generally favored as candidates. Moreover, ectopic activity in the PV may not be present during the electrophysiologic study, even when provocative pharmacologic or pacing procedures are performed. The electroanatomic study by Pappone et al may be helpful in these types of cases. They developed an anatomic approach aimed at isolating each PV from the left side of the atrium (LA) by circumferential radiofrequency (RF) lesions around their ostia. With use of a nonfluoroscopic mapping system, they generate 3-dimensional electroanatomic LA maps and deliver RF energy to the vulnerable sites.

In view of the difficulties in producing effective lesions when there are multiple PVs, ablation of arrhythmogenic PVs is currently indicated in patients with symptoms of paroxysmal AF that is multidrug-resistant. In such cases, the risks associated with persistent AF (notably, 1%-3% thromboembolic events per year with increased mortality) and the risks of antiarrhythmic and anticoagulant drugs appear to outweigh those of the ablation procedure. In addition, this approach is clearly superior to atrioventricular junction ablation. A history of thromboembolic phenomena or tachycardia-mediated heart failure, as evidence of AF morbidity, also strengthens the indication for the procedure.

PV ablation in chronic AF

In chronic AF, the role of substrate that maintains AF is more dominant than that of trigger foci. Consequently, many studies have resulted in AF recurrences after cardioversion and have demonstrated the efficacy of ablating these foci of reinitiation.

Lau et al performed mapping of AF reinitiation in 32 patients with chronic AF (mean, 13 months) and identified a PV focus in 4 patients. In a study by Haissaguerre et al, the conditions of 15 patients, 7 with structural heart disease and persistent AF, were observed for 5 ± 4 months. In all patients, cardioversion was followed by documentation of P-on-T pattern and/or early recurrence, which allowed mapping of the reinitiating trigger. A total of 32 arrhythmogenic PVs and 2 atrial foci (left-sided septum and appendage) were identified. No PV stenosis was noted either acutely or at repeated follow-up angiography. In total, 8 patients (55%) had stable sinus rhythm without antiarrhythmic drugs with a follow-up of 11 ± 8 months, and the use of anticoagulants was terminated in 7 patients. The successful outcome was associated with PV potential elimination. As previously discussed, Pappone et al reported a new anatomic approach for curing AF by circumferential RF ablation of pulmonary vein ostia. Twenty-six patients with resistant AF, either paroxysmal (n = 14) or permanent (n = 12), were selected; 18 (69%) of these patients had no structural heart disease. Patients were followed-up closely for
6 or more months. Among 14 patients experiencing AF at the beginning of the procedure, 64% had sinus rhythm restoration during ablation. PV isolation was demonstrated in 76% of 104 PVs treated with low peak-to-peak electrogram amplitude inside the circular line and by disparity in activation times across the lesion. After 9 ± 3 months, 22 patients (85%) were AF-free, including 62% not taking and 23% taking antiarrhythmic drugs, with no difference (P = NS) between paroxysmal and permanent AF. No thromboembolic events or PV stenoses were observed by transesophageal echocardiography. However, this study was limited by a selected group of young patients who had no structural heart disease, normal LA size, and good cardiac function. A larger group and longer follow-up are needed to further investigate the role of trigger ablation in curative therapy for chronic AF.

**PV ablation success**

Haissaguerre et al\(^{54}\) reported that elimination of the PV potentials correlated better with clinical success than did acute ectopy suppression. The success rate depends on the number of arrhythmogenic PVs (from 93% in patients with a single arrhythmogenic PV to 73% and 55% when 2 or more PVs were involved) because of the difficulties in consistently eliminating the PV potential (Table II). A single PV is significantly associated with younger patients, fewer attacks of AF, and smaller atrial dimensions, whereas multiple arrhythmogenic PVs are associated with older patients with a longer history of AF, more frequent episodes, and larger atrial dimensions. Most of the conditions of patients with unsuccessful outcomes were significantly improved with previously ineffective drugs. Chen et al\(^{44}\) reported an 86% success rate in 79 patients who had short episodes of AF (daily duration, 28 ± 30 minutes). Multiple PVs were found in only 44% of patients, and their procedural end point was acute ectopy suppression without relying on PV potential mapping.\(^{49}\)

As previously discussed, ectopic activity may arise in more than 1 PV; that was the reason Pappone et al\(^{52}\) isolated each PV by creating circumferential RF lesions around their ostia. They reported a
73% (n = 19) discharge rate without the need for antiarrhythmic drugs. Of the remaining 27% (n = 7), the administration of amiodarone was maintained for 4 patients because of other arrhythmias, and 3 who had in-hospital AF episodes were given a previously ineffective antiarrhythmic drug.

**Complications**

PV stenosis, defined as a diameter reduction of 50% or more, was observed. Distal PV narrowing as great as 42% in cases of unlimited RF power was detected. The limitation of RF power to less than 30 watts resulted in no ostial PV stenosis (although it occurred in a branch). This limited power was associated with low “achieved” temperature in the PV (average, 42°C) because of the local high cooling blood flow similar to the functioning of the irrigated tip catheter, resulting in considerably decreasing the incidence of extracardiac damage. Pappone et al reported no cases of PV stenosis with circumferential ablation, probably because lesions were made 5 mm or more apart from the ostia, thereby preventing scarring and contraction of the venous wall that resulted from thermal injury.

Other potential risks of left atrial ablation procedures are less specific, including hemopericardium (1%), thromboembolic events (1%), and other catheterization side effects.

Tsai et al reported profound bradycardia-hypotension response that was induced by RF ablation of the PVs. The Bezold-Jarisch-like reflex might have been the underlying mechanism for this.

**Limitation of PV ablation**

Kay discussed the potential of limitations, including technique difficulty, complications, and the nature of the arrhythmia. First, the ablation procedure is time-consuming, and the electrophysiologic mapping is relatively crude by current technique. These considerations limit the ability to ablate the trigger foci of AF. Second, the 3-dimensional anatomy of the PVs is complex and variable among individuals. As a result, it may be technically difficult to precisely map and ablate the initiating trigger origin. Third, there are complication limits of RF applications.
current due to thermal injury and PV stenosis, from either acute spasm or chronic fibrosis. Fourth, AF is an acquired and progressive condition; therefore, patients may require repeated ablation procedures or further antiarrhythmic drug therapy. Finally, in patients with chronic AF, it is difficult to restore sinus rhythm and to map for initiating foci.

**New energy source for ablation**

Wellens\(^{59}\) reported on new energy sources for ablation. Currently, most physicians report experience with RF energy. Many studies are evaluating the appropriate RF power, heat limits, pulsed versus continuous RF energy delivery, and the use of irrigated-tip RF ablation. The purpose is to produce a homogenous lesion that does not complicate the PV structure and the nearby extracardiac tissues. Therefore, new energy sources for ablation are being developed, such as ultrasound delivered through a balloon in the pulmonary vein,\(^{60,61}\) laser, and cryo-ablation. Advantages and disadvantages of these energy sources for ablation should be analyzed and compared both in the clinical outcome and in the histopathologic level.

**Ideal catheter ablation for AF**

Because of technique, equipment, results, and complications of catheter ablation, new technologic development is under way. To be established as a first-line therapy for AF, the efficacy of catheter ablation should be superior to that achievable with standard antiarrhythmic medications. Kay\(^{58}\) concluded that the procedure must also be at least as safe as long-term antiarrhythmic drug therapy. The ideal ablation technology should be effective in restoring sinus rhythm and preventing recurrences of AF for long term. The procedure should be less lengthy than that of the current process (not more than 3-4 hours in the electrophysiologic laboratory). Moreover, the complication rates should be low, including thromboembolic events before or after the ablation process. The occurrence of PV injury and extracardiac damage should also be low. If these requirements are possible through technologic development, catheter ablation will be the therapy of choice for many patients with AF. Eventually, this strategy will be performed on a widespread basis, provided that the technique is simple, safe, practical, effective, and economical, as proved by ongoing studies.

**CONCLUSION**

Patients with symptomatic paroxysmal AF who have drug-resistance or drug-intolerance are indicated for this curative ablation. However, selected patients with chronic AF are also considered to be candidates. Nevertheless, recurrence of AF and complications of ablation are the main concern, leading to careful selection of appropriate patients. With newer knowledge and technologies, more and more patients with AF will undergo treatment with PV ablation. Although 89% to 96% of AF triggers have been shown in the PV, the arrhythmia can be initiated by ectopy from the other veins, crista terminalis, coronary sinus ostium, and atrial free wall. Therefore, one limitation is that the trigger foci of AF may not be from the PV in origin.

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