New Approaches to the Management of Atrial Fibrillation
The Role of the Atrial Defibrillator

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Atrial fibrillation (AF) is the most common arrhythmia for which patients are hospitalized. It imposes important morbidity and mortality on patients’ lives, engendering enormous expenditures for its management. The frequency of AF increases with age (10% in patients >70 years old) and with the presence of congestive heart failure (up to 25%). Clinically, the appearance of AF may be associated with a variety of symptoms, including palpitations, heart failure, syncope, and chest pain, which occur primarily because of the heart rate. In addition, AF imposes an important risk of thromboembolism and the potential for the development of tachycardia-mediated cardiomyopathy. It has been estimated by some that nearly 40% of strokes in patients with AF are secondary to atrial thrombi. Thus, in my opinion, the most desirable therapy would be the use of some therapy that maintains sinus rhythm and eliminates the need for anticoagulation. This is supported by a Markov model of AF management.

Because drugs have shown limited efficacy and significant side effects, interest in the development of nonpharmacological therapy for AF has arisen. At the present time, ablation of the AV node with pacemaker implantation is an accepted form of rate control that definitely works, is associated with hemodynamic benefits, and does not require drugs, with their attendant side effects. This form of therapy, although it is usually used for drug-refractory cases, may in fact become a procedure of choice in patients who need pacemakers because of brady-tachy syndrome and, in particular, those who have cardiomyopathies and AF with rapid responses, in whom β-blockers and calcium blockers may be more detrimental to their hemodynamic function. In patients with the sick sinus syndrome, atrial pacing has been shown to be beneficial compared with ventricular pacing for prevention of the development of chronic AF, decreasing mortality and thromboembolic events. More recent data suggest that dual-site right atrial pacing, bicameral pacing, and coronary sinus pacing alone may be more useful in preventing AF than high right atrial rate pacing alone.

The poor success of maintenance of sinus rhythm with drugs and subsequent thromboembolic sequelae have even led to the development of a surgical procedure (the maze operation) that compartmentalizes the atrium so that it cannot fibrillate. Although this procedure can achieve sinus rhythm, it carries with it significant morbidity, and the actual hemodynamic and anti-thrombotic benefits of sinus rhythm with abnormal atrial contraction are not clear. Catheter techniques are also currently being used to mimic the maze procedure. These procedures have significant morbidity and an unknown success rate of maintaining sinus rhythm. At this time, they should be considered experimental. Recent observations have demonstrated that focal atrial tachycardias or atrial premature complexes can precipitate some cases of paroxysmal AF. In such instances, these atrial tachycardias and/or atrial premature complexes have been successfully ablated and prevented AF. Other investigators have demonstrated that a combination of drugs that convert AF to atrial flutter combined with a simple flutter ablation can restore and maintain sinus rhythm and does not result in impaired atrial function.

Over the past several years, evidence has accumulated that electrical and anatomic remodeling of the atrium occurs during the initial periods of AF. This has led to the concept that AF begets AF, which in turn suggests that early restoration of sinus rhythm might decrease the recurrence rate of AF or even, in some cases, prevent its recurrence. About the same time, it was demonstrated that internal cardioversion could successfully restore sinus rhythm in patients in whom external cardioversion could not. Although these initial studies required high energies delivered between a lead in the right
atrium and a patch on the chest. Levy et al subsequently demonstrated that low-energy (3-J) shocks between a right atrial and a coronary sinus coil using biphasic waveforms could convert AF, particularly when it was present for \(<1\) year. These findings led to the concept of an implantable atrial defibrillator that could restore sinus rhythm rapidly by use of low-energy shocks, thereby leading to maintenance of sinus rhythm for greater periods of time, lowering the thromboembolic complications of AF, and decreasing the negative effects of AF on cardiac function.

In this issue of Circulation, Wellens et al present the first experience with an implantable atrial defibrillator (Atrioverter) as a method of converting AF to sinus rhythm. This multicenter, nonrandomized study was undertaken to evaluate the efficacy, safety, and potential utility of this device in patients with AF at low risk for ventricular arrhythmias. This trial involved 19 sites, from which only 51 patients met inclusion criteria. In this highly selected patient group, the Atrioverter, which was manually activated by a physician, was able to achieve sinus rhythm for at least a brief period of time in 96% of patients with AF. However, early recurrence of AF within seconds to minutes was observed in 26% of episodes (62) in 21 of the 41 patients who had AF. This was able to be treated successfully with the device, with the addition of intravenous or oral antiarrhythmic agents in 36 patients. The remaining 26 episodes required either external countershock, subsequent intravenous drug administration, or allowance for late spontaneous conversion. The overall success rate of the device for cardioversion to stable sinus rhythm with or without additional drugs was 86%. The number of shocks required to successfully terminate AF is difficult to ascertain. Although 670 shocks were given for 227 episodes (3 per episode), it is unclear in how many patients the first shock was successful. Up to 8 shocks were delivered for the acute failures or earlier recurrence of AF.

There was a rather high complication rate in this trial: subclavian vein thromboses (\(n = 2\)), tamponade (\(n = 1\)), and requirement for right atrial lead repositioning for lead dislodgment (\(n = 1\)) or increasing defibrillation thresholds with inability to successfully convert AF (\(n = 3\)). There was 1 ventricular lead dislodgment. In all cases, the leads could be successfully repositioned with adequate defibrillation thresholds. In 1 patient, the system was removed because of frequent episodes and shocks and was replaced by a standard dual-chamber pacemaker after this bundle ablation. In another, it was removed because of infection. Although the high incidence of complications seems remarkable, it is somewhat reminiscent of the early experience with ICDs. Of importance is that there were 19 sites, some of which had only 1 patient included. If only sites with larger experiences were included, the effect of a “learning curve” would be seen. In 1 center that has implanted 16 systems and has a large pacemaker and ICD experience, there were no dislodgments and no failures (Hein Wellens, MD, oral communication, July 1998). Thus, experience as with the implantable Atrioverter and other systems significantly affects outcomes. Efficacy was hard to evaluate from the data presented. Although the device can convert AF (96% successfully), a large number of patients (52%) needed multiple shocks and/or drugs due to early recurrence of AF, and 26 episodes subsequently required an additional intervention or allowance of spontaneous cardioversion. These findings stress an important limitation of the use of the system as an automatic device. In this study, all patients underwent initiation of therapy by a physician for the first 3 months, after which the patient could activate the devices themselves. This is usually done at home. It is possible, however, that in this type of patient population (ie, low ventricular arrhythmia risk), the device may be initially programmed in the automatic mode. If automatically delivered therapy fails, subsequent therapy can be initiated in a doctor’s office, emergency room, or arrhythmia clinic. In either instance, the Atrioverter would decrease hospital admissions and associated costs of inpatient cardioversions. Safety has been a big concern, but in this low-risk group, 670 shocks given for 227 episodes of AF and 3049 shocks given during testing were not associated with any ventricular proarrhythmia. This is primarily because therapy can be delivered only after a 500-ms RR cycle. The sensing algorithms also were fine, with 92.3% of AF being recognized as AF. More importantly, the system was 100% specific, ie, sinus rhythm was recognized as sinus rhythm. The atrial defibrillator needs to err on the side of being specific so that it does not give inappropriate shocks for a nonlethal arrhythmia, in contrast to ventricular defibrillators, which must err on the side of being too sensitive so that lethal ventricular arrhythmias are not missed. Another issue that needed to be addressed was patient tolerance. In this study, patient tolerance appeared to be good, particularly for the first shock. It has been shown that patients tolerate the first shock quite well; tolerance diminishes and sedation is required only with increasing numbers of shocks. Subsequent unpublished data from Wellens’ laboratory (oral communication, July 1998) and others are all consistent with this initial experience.

Several issues need to be addressed regarding the potential role of the Atrioverter. The present study demonstrates that it can successfully convert AF to sinus rhythm, that in this low-risk patient population there was no ventricular proarrhythmia, and that it is generally well tolerated. However, it is unclear which patients are appropriate candidates for such a device. Only 51 patients were selected in 19 centers, suggesting a large bias in patient selection. One needs to know how these patients were selected and what the clinical presentation of AF was: paroxysmal AF, persistent versus chronic AF. It is stated that the 51 patients came from 119 patients who were screened. This suggests that successful cardioversion at 260 V can be achieved in only 43% of patients in whom it is tested. The question that was not addressed is to define the population in which the screening process would be initiated. This would help define the population in whom the Atrioverter might be a valuable therapy. People with paroxysmal AF are probably poor candidates because of their very frequent nonsustained, short-lived episodes of AF, which would require too many shocks from the device. People with chronic AF of \(\geq 1\) year’s duration are probably also not ideal candidates.

What is the future role of an atrial defibrillator? Recent advances have suggested that atrial pacing may prevent AF and that either dual-site, bicameral, or coronary sinus pacing alone may be beneficial. A natural evolution of the current
Atrioverter would be to have pacing capability in addition to defibrillation capability. The combination of a device capable of dual-chamber pacing and atrial defibrillation, with or without pharmacological pacing, will increase the patient population in whom the Atrioverter could be used and ensure a higher incidence of prevention of AF. The concept of atrial defibrillation is also applicable to patients with primary ventricular arrhythmias who also have AF. Perhaps 5% to 20% of patients requiring ventricular ICDs have coexistent AF. A combined atrial and ventricular defibrillator system with dual-chamber pacing might be very useful for this group of patients. Such a device, the Jewel AF, is available in Europe as an investigational system. It is unclear what type of device should be used in patients who have a substrate for ventricular arrhythmias but have never experienced an episode. The Atrioverter has a high safety record in patients without a known ventricular arrhythmia substrate, but it is not known how safe it will be in patients with organic heart disease. The manufacturer is now doing a similar study of the Atrioverter in patients with organic heart disease but without prior ventricular arrhythmias to assess its safety in such patients. Whether or not this device alone will be safe or whether such patients will require ventricular defibrillation backup is unknown.

In summary, it is clearly established that low-energy internal cardioversion can successfully convert AF to sinus rhythm. Time will tell whether early conversion of sinus rhythm will actually decrease the frequency of AF, and we are awaiting data about this important outcome. Concerns will always exist related to costs, efficacy, and safety in all patient populations, as well as tolerability, particularly in patients who have high defibrillation thresholds and require multiple shocks. Present indications for the device include recurrent symptomatic, drug-refractory AF in patients in whom the Atrioverter could be used and ensure a higher incidence of prevention of AF. The Framingham Study. Stroke. 1995;22:983–988.

References

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