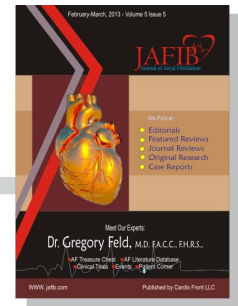




Featured Review

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## Is An Atrial Defibrillator Still An Option In Treating Patients With Atrial Fibrillation?

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### Abstract

Atrial fibrillation (AF) is a common disorder associated with significant morbidities and presents several challenges for the control of symptoms and prevention of long-term implications. Atrial defibrillators (ADs), used for rhythm control in patients with symptoms refractory to medical therapy, can detect recurrences of the arrhythmia, allow prompt patient-directed treatment, and have the potential to reduce hospitalizations and improve quality of life. The efficacy of this form of therapy is highest in patients with paroxysmal AF, and with the use of a coronary sinus shocking lead. While R-wave synchronized shocks are a prerequisite for a safe use, the procedure is well tolerated and usually not associated with long-term psychological side effects. Limitations of ADs include acute and chronic complications related to cardiac rhythm device implantation, the requirement in some cases for more than one shock to terminate AF, the discomfort from shocks, as well as the need for sedation to alleviate pain from the shocks. With the ever-expanding role of catheter-based therapies for AF, it seems that the role of ADs in this regard is rather limited.

### Introduction

#### Background

Atrial fibrillation (AF) is the most common arrhythmia seen in clinical practice and has several unfavorable implications, mostly systemic and cerebral embolism, reduced cardiac output and death.<sup>1-3</sup> Symptoms related to AF include palpitations due to irregularities in the heart rate, and hemodynamic impairment due to reduced stroke volume related to the loss of atrial contribution to ventricular filling. The cornerstones of the management of AF are treatment of symptoms related to irregular heart rhythm and reduced stroke volume

as well as thromboembolism prophylaxis. While rhythm and rate control are considered equivalent in terms of long-term clinical end points,<sup>4,5</sup> maintenance of sinus rhythm is sought in highly symptomatic patients. Pharmacologic therapies have been used for rhythm control but can be associated with long-term side effects as well as clinical failure. Other approaches include atrioventricular junction ablation, surgical or percutaneous radio frequency ablation, as well as device therapies such as atrial defibrillators (ADs). The latter were developed and approved before left atrial ablation became widely available. The purpose of this article is to describe the role of ADs in the current armamentarium of AF therapies.

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### Indication, Description of the Implantation Procedure and the ADs Systems

Candidate patients for the implantation of an atrial defibrillator are those with recurrent symptomatic atrial fibrillation who have failed pharmacologic therapy.<sup>6</sup> Other selection criteria exist as well, such as an acceptable number of AF episodes that would warrant implanting a permanent device, but without excessive burden resulting in repetitive therapies. An atrial defibrillator includes one or two coils in the atria and a ventricular lead for sensing and synchronization purposes. In most cases, this requires cannulation of the coronary sinus, adding another layer of complexity to the implantation procedure. In simpler configurations, standard single or dual chamber ventricular defibrillators have been used for atrial defibrillation purposes. In such systems, the shock vector configuration between the ventricle and the pectoral ICD usually includes the atria and therefore, successfully terminates atrial fibrillation. While original studies suggested that such devices have the drawback of relatively higher defibrillation thresholds, more recent ones did not find a particular advantage to CS shocking leads.<sup>7,8</sup> This approach is particularly appealing since it can be used in patients who could not receive a coronary sinus lead for technical reasons, and

would open the door for using standard ICDs for cardioversion given the high incidence of atrial fibrillation in patients with such systems. Patients with heart failure who receive ventricular defibrillators with or without resynchronization therapy may be candidates as well for atrial defibrillators, were devices with both capacities available.

Several generations of ADs were commercially available. Metrix (Incontrol – Redmond, WA) was the first such device to be developed, and had shocking leads in the right atrium and the coronary sinus.<sup>10</sup> Subsequent generations of ADs such as Jewel AF and GEM III AT (Medtronic – Minneapolis, MN) had additional features. Compared to the Metrix Activator, Jewel AF was a dual chamber defibrillator capable of ventricular defibrillation, and had the advantages of greater programmability and superior diagnostic abilities, with a patient activator for rhythm confirmation and shock delivery capabilities [Figure 1]. On the other hand, GEM III AT was a dual chamber defibrillator that shared many of the features of Jewel AF, but did not include a coronary sinus lead.

### Efficacy

While electrical cardioversion of atrial fibrillation is usually performed by applying energy across the

**Figure 1:** Medtronic Jewel AF Atrial Defibrillator and Patient Activator<sup>32</sup> (with Permission)



chest, endocardial leads can be used to terminate AF, with some evidence suggesting that it is effective in patients who fail external cardioversion.<sup>11</sup> It is also well known that patients with ventricular defibrillators receive inappropriate shocks due to rapidly conducted AF, and multi-programmable dual chamber ICDs can discriminate between supraventricular and ventricular tachycardia and terminate AF by pacing.<sup>12</sup> The efficacy of using low-energy atrial cardioversion has been evaluated in several studies that included patients with persistent or paroxysmal AF, as well as those with structural heart disease and reduced left ventricular function.<sup>13</sup> When studied in the electrophysiology lab, the success rate of conversion to sinus rhythm is 70% in cases of persistent AF, and up to 90% with paroxysmal AF, using catheters in the right atrium and either the coronary sinus or the branch pulmonary artery.<sup>14,15</sup> The recurrence rate, on the other hand, is not minimal and can be as high as 37% over an average follow up period of 9 months. Energy requirements for successful cardioversion differ among the different subsets of AF, ranging from 1.8 J for paroxysmal AF to 3.6 J for persistent AF.<sup>15</sup> Other factors that are associated with lower energy requirements include shorter duration of AF, smaller left atrial size, absence of structural heart disease, higher left ventricular ejection fraction, and smaller left ventricular cavity dimensions.<sup>14,15</sup> Delivering sequential biphasic waveforms over dual-current pathways can lead to lower defibrillation threshold as well.<sup>16</sup>

Using ADs to deliver R-wave synchronized shocks as a long-term treatment strategy for recurrent drug-refractory AF is successful in 90-95% of cases.<sup>17</sup> Approximately 27% of episodes require more than one shock, and an average of 1.6 shocks is needed per episode for termination.<sup>10,17</sup> Determinants of first-shock success are the use of a coronary sinus electrode, absence of a class III anti-arrhythmic drug, and the absence of early recurrence of AF.<sup>18</sup> It is notable that early cardioversion (within 3 hours of onset of AF) was a negative determinant of first shock success in some studies,<sup>18</sup> but when taking into account episodes that have lasted for weeks, the longer the waiting time, the higher the required energy for successful cardioversion.<sup>19</sup> Atrial anti-tachycardia pacing is generally considered a poor strategy to terminate atrial fibrillation, with the GEM III AT ICD able to terminate AF in only 26% of cases.<sup>20</sup> 50 Hz

atrial burst pacing does not seem to add much additional benefit with success rates of 25-30%, and a worse result if the atrial cycle length is less than 160 ms.

Terminating AF with these devices translated into an improvement in symptoms, quality of life and ability to perform physical activities, as well as a reduction in arrhythmia-related hospitalizations.<sup>21</sup>

## Safety

From a safety standpoint, ventricular arrhythmias are rarely induced when shocks are synchronized, even in patients with history of ventricular tachycardia and left ventricular dysfunction. Rare episodes of ventricular fibrillation (VF) have been induced in cases of T wave oversensing, shock administration during ventricular-paced rhythm or ventricular tachycardia (VT). Cardioversion of AF using low-energy R-wave synchronized shocks is therefore considered safe, if delivered during narrow-complex rhythm, even in patients with history of VT.<sup>17,22</sup> One other potential safety concern is the development of post-shock bradycardia in up to one third of patients. Since these devices are capable of dual chamber pacing, this issue poses minor clinical consequence.

## Benefits and Limitations

In addition to symptom control, advantages of implanted ADs are the ability to perform cardioversion in the outpatient setting, at a time that is socially and physically acceptable, and possibly without the direct involvement of a health care professional. Thus, it avoids hospitalization, empowers patients to control atrial fibrillation symptoms, and allows for their direct participation in the health delivery process. The projected effects are improvement in quality of life and health care savings.

On the other hand, implanted devices can have specific disadvantages that can be divided into immediate and long-term limitations. Immediate disadvantages include infection and mechanical complications from the implantation procedure such as pneumothorax, cardiac perforation and tamponade. The rate of such complications can be as high as 4%.<sup>17</sup> In the long term, there is the

possibility of inappropriate shocks, the discomfort from appropriate discharges, and vascular complications such as venous occlusion. Clinic visits are also required on a regular basis for device monitoring and management. It should also be noted that appropriate anticoagulation must be maintained at all times since cardioversion can be performed at any moment, and theoretically should be stricter than in the general population of patients with atrial fibrillation. Not all patients receiving atrial defibrillators for recurrent, symptomatic and drug-refractory AF can be transitioned to an ambulatory delivery of shocks and most patients do not become free of anti-arrhythmic medications.<sup>17</sup>

Other limitations include shock failures, AF storms leading to repetitive shocks, unexpected shocks if the device is programmed to automatically treat AF, treating asymptomatic episodes (asymptomatic AF burden may be as high as 10-fold compared to symptomatic episodes), inappropriate diagnosis of ventricular arrhythmias due to far-field R wave sensing or misclassification of rapidly conducted AF as ventricular fibrillation.

The long-term psychological and physical effects are applicable to any implantable device and include physical concerns, driving restrictions, over-protectiveness from family, requirement for generator changes, and potential for device malfunction and recalls. It has been estimated that many patients who receive ventricular defibrillators develop symptoms of anxiety and depression post implantation. While this has not been shown in patients with atrial defibrillators and no correlation was seen between shock frequency and development of anxiety, this could be due to the relatively smaller number of patients studied and may also be related to the fact that ICD shocks are less predictable and are used to treat life-threatening arrhythmias.

The efficacy of beta-adrenergic blocking agents for rate control in AF and maintenance of sinus rhythm after cardioversion is well-established.<sup>17,18</sup> However, their role in the primary prevention of AF is less defined. Maladaptive adrenergic stimulation is postulated to contribute to the electrophysiologic and structural atrial remodeling mechanisms that initiate and perpetuate AF.

Blunting this excessive sympathetic response, in theory, may help prevent the development of this disease.

### Tolerability and Means to Improve it

Pain perception is one of the main factors that affect the widespread use of the atrial defibrillator. The type of pain that patients perceive is described as a dull sensation in the anterior chest that is relatively short-lived, typically disappearing within 30 seconds.<sup>9</sup> Pain level usually correlates with increasing voltage, with marked inter-individual variation.<sup>14,23</sup> It is unusual that sinus rhythm is restored before the tolerability threshold is reached. In one study, the average discomfort score was 5.2 on a 1-10 scale for successful therapy, and was slightly lower for unsuccessful therapy. As expected, satisfaction score was much higher for successful therapy.<sup>10</sup> The vast majority of patients perceive shocks of 3J or more to be intolerable.<sup>24</sup> In a different study, patients were usually unable to distinguish between shocks of 0.4 to 2 J and perceived the shocks as uncomfortable and rated the second shock as more painful irrespective of the actual energy level. Still, more than 80% of patients mention that they would tolerate such shocks at a rate of one per month and around 45% felt a weekly shock is acceptable. This implies that patients are willing to accept the shocks for symptomatic treatment as long as the number of shocks needed to terminate each episode is minimized and the discharges are infrequent.<sup>25</sup> In the majority of cases however, only few patients tolerate internal cardioversion while fully conscious.<sup>23</sup>

Since pain perception is a major impediment, achieving an atrial defibrillation threshold that is lower than the discomfort threshold is of paramount importance. Unfortunately, this is rarely feasible. In many instances, it has been shown that the comfort threshold is 0.1 joules or more, which is considerably lower than the atrial defibrillation threshold of implanted devices. To alleviate this burden, adjunctive therapies such as antiarrhythmic medications to decrease the defibrillation threshold, manual controllers for self-administration of shocks, programming nocturnal therapies or even using self administered premedication may be needed, each approach with its own limitations. Automatic nighttime cardioversion has been shown to be effective and is generally well tolerated, but

many patients are not suitable for this strategy because of their irregular sleep habits with some who qualify remaining awake when the shock is administered; for some, the sleep pattern may become disrupted.<sup>26</sup> While nocturnal cardioversion may decrease the anxiety associated with the shocks, the pain perception is usually the same. Sedation is required to prevent the pain and discomfort associated with shock delivery, especially in patients who are expected to receive frequent cardioversions, and in those where therapies are administered automatically rather than by patient activation. Among the medications tried, the best approach includes a benzodiazepine, possibly combined with an analgesic. In that regard, orally administered midazolam has been shown to be the most effective due to its amnestic effect. An analgesia only strategy usually fares worse compared to sedation.<sup>27</sup> Knowing that the success of atrial defibrillation becomes markedly reduced with repeated cardioversions, and that high-energy requirements might preclude patients with long-lasting AF from receiving ADs, anti-arrhythmics have been used to lower the atrial defibrillation threshold and decrease pain perception. Both flecainide and sotalol have been evaluated in such settings. Intravenous flecainide significantly decreases the energy requirement and improves the chance of successful cardioversion in patients with AF, irrespective of the subtype. This translates into a significant reduction in pain scores in patients not using sedation<sup>28</sup> Sotalol may play a role as well in improving the chances of maintaining sinus rhythm after cardioversion. As many as 30% of patients with persistent atrial fibrillation have very early recurrence after cardioversion, and more shocks and higher energy delivery do not decrease the recurrence rate. Therefore, using medications to decrease this rate is an attractive approach. Since recurrent atrial fibrillation is triggered by premature atrial contractions (PACs) in the vast majority of cases, intravenous sotalol has been shown to decrease the number of PACs, prolong their coupling interval and prevent early recurrence in 83% of patients.<sup>19,29-31</sup> In addition, when sotalol is used after cardioversion of atrial fibrillation, the mean defibrillation threshold is decreased from 6.7 to 3.8 J using the same lead configuration. This translates into a lower sedative dose with the second procedure, as well as lower average pain score (5.1 vs. 2.7 on scale of 0 to 10).<sup>19</sup>

## Impact on Quality of life (QOL)

When the quality of life of patients with drug refractory symptomatic AF who receive ADs is followed over time, the baseline score is usually reduced compared to the general population, but all components of the questionnaire improve with time. The benefit seems to affect all patients, irrespective of whether they actually received shocks during the follow up period. While this implies a partial placebo effect, the shocks do not negate any improvement in the QOL.<sup>32</sup> Levels of anxiety and depression do not worsen and most patients mention that they would have the device implanted again.<sup>33</sup> When spouses and partners are asked, they do not have specific unfavorable opinions about the devices either.<sup>34</sup>

## Conclusions

With newer anti-arrhythmic drugs enhancing safety and efficacy, and ablation becoming widely accepted, it is unlikely that the use of ADs will increase. The need for permanent device implantation has been less attractive, particularly in younger patients, due to long-term considerations such as chronic risk of infection, vascular complications, device longevity, and avoidance of magnetic resonance imaging. These issues are more acceptable with ventricular-based ICDs given the life-saving potential of such devices; atrial-specific defibrillators lack this benefit. Evidence comparing outpatient cardioversion versus ADs is lacking, and cost, convenience, and patient acceptance would need to be directly compared, but this is unlikely to happen. The 2011 ACCF/AHA/HRS guidelines for the treatment of atrial fibrillation do not present a specific set of recommendations for their use, and acknowledge that only a small subset of patients may benefit from them.<sup>36</sup> In our opinion, ADs may have a specific role in those with recalcitrant, paroxysmal AF where other treatment strategies have failed, and in those who are willing to undergo unsedated, self-administered cardioversion. Given that a very small population would derive benefit from ADs, it is uncertain if manufacturers would continue to offer such therapy in their future product lines. The most feasible approach would be to incorporate ADs in standard ICDs or cardiac resynchronization devices, though this may be

what some would consider a prohibitively expensive approach. Despite these limitations, research in this field remains active.<sup>37-40</sup> Consideration for future therapies may include devices directed towards more tolerable therapy such as those offering superior shock waveforms (allowing lower shock energy/voltage) or novel pacing strategies to effectively suppress AF triggers. Such innovations may ultimately allow for a revival of these devices.

## Disclosures

No disclosures relevant to this article were made by the authors.

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