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Role of Bi-Atrial Pacing In Slowing The Progression of Paroxysmal Atrial Fibrillation To Permanent Atrial Fibrillation

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Abstract

Introduction: Bi-atrial lead placement combined with atrial overdrive pacing has demonstrated a reduction in percent time mode switched and mode switches per day. This retrospective analysis compared long term outcomes of patients with right atrial overdrive pacing alone (DAO) to patients having atrial overdrive with bi-atrial leads (BIA) in slowing the progression of paroxysmal atrial fibrillation (PAF) to permanent continuous atrial fibrillation (CAF).

Methods: Thirty-three patients age 76.6 (+/-1.96) from our prior investigation were selected. The DAO control group (N=16) had received a standard right atrial pacing lead. The BIA group (N=17) had pacing leads placed in the right atrium and coronary sinus. Patients were followed for a mean 1217 days (+/-838). Days of CAF was classified as the date of final mode switch until analysis.

Results: A total of 40,171 follow-up days were evaluated. The mean follow-up for both cohorts was 1217 days (+/-838). The DAO group consisted of 15,318 days (mean 957 +/-761) and the BIA group 24,853 days (mean 1461 +/-854). A lower total number of days were spent in CAF in the BIA group versus the DAO group, 1380 vs 2197 respectively. Corrected for follow-up duration, 5.55% days in CAF was seen in the BIA group vs. 14.34% in the DAO group which did not reach statistical significance. .

Conclusions: Although BIA overdrive pacing initially demonstrated reduced time in mode switch compared to DAO alone, this analysis did not detect a reduction in progression to CAF. More subjects or a longer follow up would be needed.

Introduction

Atrial fibrillation (AF) continues to be one of the most commonly observed supraventricular tachy-arrhythmias observed in clinical practice. In the general population, the Framingham Heart Study[1] found the prevalence of AF in the United States to be approximately 2.2 million persons. The worldwide incidence has been suggested to be well in excess of 5 million.[2] Rhythm control continues to be an appropriate strategy for patients with symptomatic paroxysmal atrial fibrillation (PAF). In many recent trials, differences between rhythm and rate control strategies seem to be similar in outcomes ranging from death and hospitalization[3,4] to systemic embolization.[5] One of the largest trials comparing these two arms, Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM),[6] showed that the presence of AF had a marked impact on NYHA functional class.[7] Additionally, the 6 MHW distance seemed longer in the rhythm control group, a finding similar to that in the Pharmacological Intervention in Atrial Fibrillation (PIAF) trial.[8] These factors may lead to a clinical preference to maintaining rhythm control for patients for as long as possible.

In our previous investigation, we evaluated patients with an atrial overdrive pacing algorithm enabled as a control and compared their outcomes to a bi-atrial pacing group with the same feature enabled.[9] This data demonstrated not only a reduction in percent time mode switched, but also a lower rate of mode switches per day. [Table 1] Although many of these modalities have demonstrated some benefit in decreasing the clinical incidence of paroxysmal atrial fibrillation, little has been reported on the ability of combined therapies and their efficacy in preventing the evolution of PAF to permanent atrial fibrillation.

The goal of this analysis was to determine if bi-atrial pacing in conjunction with an atrial overdrive algorithm could slow the progress from paroxysmal to permanent atrial fibrillation.

Subjects

The Deborah Heart & Lung center database was queried to create a retrospective analysis of a specific patient population evaluating two pacing interventions and their effect on slowing the progression of PAF to CAF. A total of 33 patients having a standard indication for permanent pacemaker implantation as per American Heart

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None.

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Table 1: Comparison of Groups: RA=Right Atrial; LA=Left Atrial

	Table II. Group Comparisons		
	Control	Bi-Atrial	
Subjects (n)	16	17	
RA lead threshold	0.99 ± 0.15 V	0.81 ± 0.07 V	
Pulse width	0.5 ± 0 ms	0.92 ± 0.06 ms	
LA lead threshold	-	2.81 ± 0.21 V	
Pulse width	-	0.92 ± 0.06 ms	
Atrial lead impedance	501 ± 19.9 Q	335 ± 10.9 Ω	
Total days followed	546.3±95.8	265.5±51.4	
Mean total mode switches*	885.4 ± 472.6	108.6± 57.2	*P = 0.03
Mean mode switches per dayt	4.40±3.24	0.62 ± 0.43	fP = 0.06
Percent time in mode switch* *	18.2 ±7.2	0.6 ±0.1	**P = 0.014

Association / American College of Cardiology guidelines were selected for analysis. In addition, at implant these patients were screened and required to have documented PAF as reported in the initial investigation.[29] Patients were included only if they had the Dynamic atrial overdrive (DAO) algorithm enabled at the time of implantation and its programming and detection standardized as discussed later. These patients were then divided into a control group consisting of patients with a single right atrial lead placed in the region of the atrial appendage (DAO group). These patients were compared against patients with dual atrial placed leads (BI-A group), one in the right atrial appendage region with the other placed into the body of the coronary sinus. All patients also had a lead placed into either the right ventricular (RV) apex or outflow tract.

Implantation

At device implantation, a standard implant technique was utilized to introduce and position a lead into the RV apex or outflow tract for ventricular pacing. In the DAO group, a lead was placed in the area of the right atrial appendage. In the BI-A group, a second lead was introduced utilizing a formed stylet, into the mid to distal coronary sinus. [Figure 1] A model 1488 (St Jude Medical, Sylmar, CA, USA) was utilized without extension of the helix and the active pacing collar used as the cathode. The lead was then Y-adapted to the right atrial appendage lead to share the anodal portion and complete the circuit utilizing an Oscor (Guidant Corp. St Paul, MN, USA) adapter. Pacing, sensing, capture, and resistance was assessed through a pacing system analyzer and confirmed utilizing the P wave morphology on surface electrocardiogram (ECG) as well as the custom intracardiac electrogram channel.

Standardized Programming

Patient selected for analysis were implanted with St Jude Medical Identity® or Integrity® devices (St Jude Medical Sylmar, CA, USA). As the DAO algorithm was critical to our analysis, one manufacturers DAO algorithm and device programming specific to this feature was selected and verified to be consistent through the duration of the analysis. All patients had a programmed base rate of 60 bpm, with AF Suppression™ pacing feature (DAO) programmed to ON in both groups. Each was programmed at 15 cycles with the maximum sensor rate serving as the ceiling and programmed to 90 bpm. The overdrive rate is determined by a lookup table. [Table 2] In order to determine when a patient enters atrial fibrillation, these particular devices utilize a programmable rate, or Atrial Tachycardia Detection

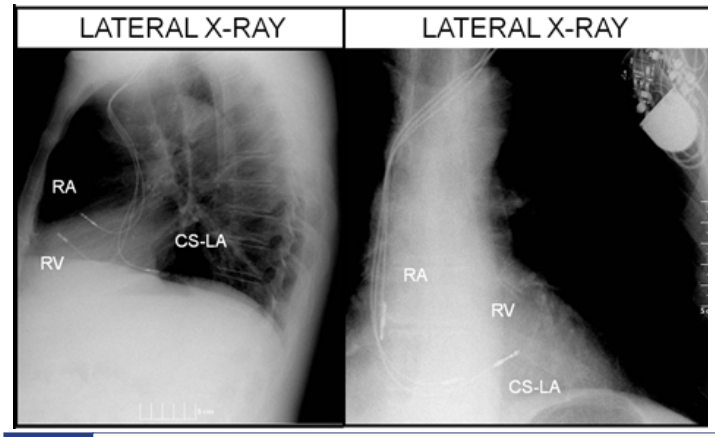

Figure 1: Chest radiographs showing biatrial pacemakers in situ. RA=Right Atrial; RV=Right Ventricle; CS-LA=Coronary Sinus lead pacing the Left Atrium

rate (ATDR) to determine the rate in which the device classifies episode. Automatic Mode Switch (AMS) occurs in the presence of a sustained atrial rate. This is determined utilizing an algorithm which calculates a Filtered Atrial Rate Interval (FARI), which compares a current rate to a running rate average. When the FARI exceeds the ATDR, in this case 180 bpm was selected, the device switches to the programmed non-tracking mode. This standardization in programming ensured both the function and recording of atrial fibrillation was consistent between the groups.

Statistical Analysis

Means, medians, and percents were reported for baseline clinical variables and calculated for the entire cohort. Continuous variables were expressed as a mean +/- SD. Sub-analysis between lead families was performed utilizing a 2 sample T-test between percents. All tests were considered significant at a value of < 0.05. Data analysis was performed using StatPac version 3.0 (StatPac Inc. Bloomington, MN).

Results

In this evaluation the average patient's age was 76.6 +/- 1.96 years. The DAO group consisted of 16 patients, 8 male and 8 female. The Bi-A group consisted of 17 patients, 7 male and 10 female. Additionally, the DAO group contained 7 patients on Class III AAD's (Amiodarone/Sotalol) and 12 patients on Calcium channel or Beta-Blocking agents. The Bi-A group contained 6 patients on

Table 2: Overdrive Rate Conversion Table

Table I.			
Overdrive Rate Determination			
Current Rate	Overdrive Rate	Current Rate	Overdrive Rate
55	59	115	122
60	64	120	127
65	69	125	131
65	74	130	136
70	79	135	139
80	88	140	145
90	98	145	150
100	108	150	156
110	117	155	165

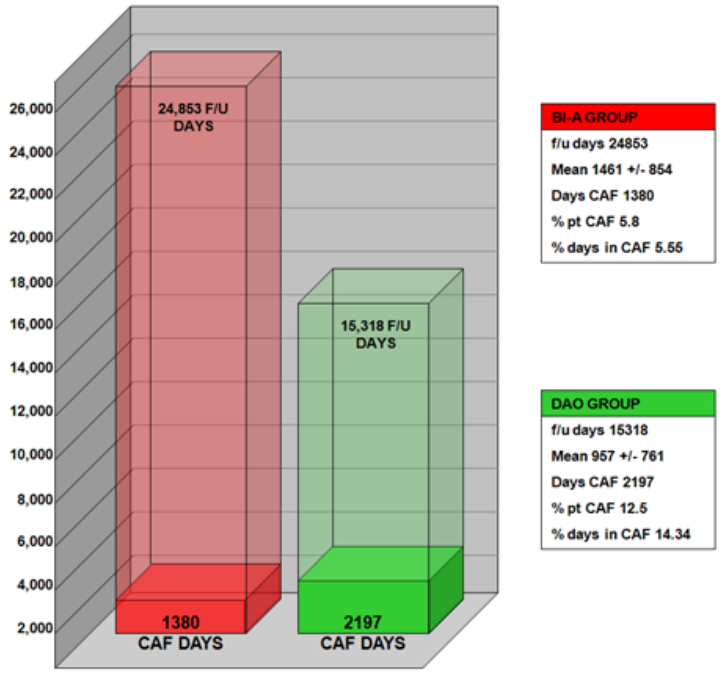

Figure 2: Follow up days vs. Days of Continuous Atrial Fibrillation. F/U=Follow up; CAF=Continuous atrial fibrillation

Class III AAD's (Amiodarone/Sotalol) and 10 patients on Calcium channel or Beta-Blocking agents. Medications remained constant thru our evaluation unless the patient progressed from PAF to CAF in which case the class III AAD was discontinued.

To control for follow-up duration variability between the groups, normalization was achieved by analyzing the percent of days in continuous atrial fibrillation (CAF). This was derived from the date of the patients final mode switch and all subsequent days until present counted as a day in CAF. We also compared the overall percent of patients who progressed to CAF. A total of 40,171 days with an average of 1217.3 +/- 838.39 of follow-up were assessed. Of these 24,853 were in the BI-A group (mean 1461 +/-854) and 15,318 in the DAO group (mean 957 +/-761). Of these days followed a lower number of days were spent in CAF in the BI-A group versus the DAO group, 1380 days vs. 2197 days respectively. [Figure 2] To correct for follow-up duration, we converted this into a percentage of total time followed in CAF, in which the BI-A group demonstrated 5.55% of days in CAF versus 14.34% days in CAF exhibited by the DAO group. (P=0.4) In addition, the number of patients who converted to CAF was different between the DAO group and BI-A group 5.6% and 11.1% respective. Although this comparison may appear clinically relevant, no statistical benefit was demonstrated between groups [Figure 3].

No adverse events, lead dislodgements, or device related complications occurred during the follow-up duration.

Discussion

The most common treatment modality to maintain rhythm control is the use of anti-arrhythmic drugs (AAD). The efficacy of AAD at one year averages about 50% for all drugs except Amiodarone which is effective about 65% of the time. For suppression of PAF, most trials suggest class IC drugs and Sotalol are equally effective and better tolerated than class IA drugs.[10-17]

As of late, current treatment modalities for PAF have also included therapeutic catheter ablation which according to the most recent internationally published data, has demonstrated success rates of 42.5% of patients without AAD, 27% with AAD, a combined success rate of 69.5% of patients followed for greater than 24 months.[18]

Pacing techniques have been proposed as an additional option to suppress PAF. Various techniques have been previously evaluated and published. The first technique, single site atrial pacing from various locations, included the high right atrium,[19] Bachman's bundle[20,21] atrial septal pacing[22-24] and the left atria via the coronary sinus (CS).[25,26] The second technique, multi-site atrial pacing, demonstrated bi-atrial pacing from the RA and CS, showing optimal suppression of PAF thru RA and distal CS pacing by Mirza et al.[26] This technique has also been investigated by others showing similar results.[19,27] The last pacing technique is atrial overdrive pacing. Most studies have yielded mixed results on the efficacy of overdrive pacing algorithms and their ability to suppress PAF as each trial had limitations in design, patient selection, and end points .[19,28-29]

Some technical limitations can be seen utilizing currently available technologies. First, as the signal is acquired from both the right atrial lead and coronary sinus lead, the separate sensed electrograms occur for each intrinsic non-paced complex. The first is a right atrial bi-pole signal, the second two both originating from the coronary sinus lead consisting of a left atrial and ventricular component from that leads bi-pole. This results in a single atrial premature complex counting 3 times towards the filtered atrial rate interval. This results in a bias towards higher percentages of AMS in the BI-A group than the control group if you are assessing just AMS. Considering the ventricular component of the CS lead is generally the largest, adjustments to sensitivity are generally not effective in eliminating overcounting. This double counting can only be alleviated with extension the device post ventricular atrial blanking periods.

In our analysis, episodes of atrial fibrillation which resolved spontaneously were not analyzed. Only episodes which progressed to a sustained episode were counted as days in CAF. In this same patient group, we previously reported a significantly lower percent time mode switched in the Bi-A group vs. the DAO group (0.59% vs. 18.2%) as well as less mode switches per day (0.62 vs. 4.40) respectively.[9] As this group was followed over time since the original publication,

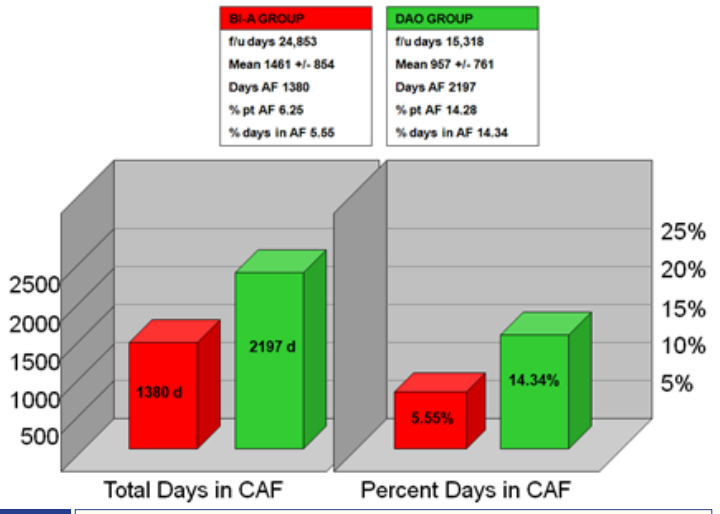

Figure 3: Atrial Fibrillation comparison between groups. d=Total Days; CAF=Continuous atrial fibrillation

valuable insight into the efficacy of combined pacing techniques may be gleaned. As the Bi-A group did not show statistical benefit from therapy, patients undergoing implantation of an additional electrode placed into the body of the CS may or may not prove beneficial in future studies. This data may provide useful insight into patients requiring CRT devices as previous data suggest that rhythm control is essential to maintaining a more functional NYHA class.[7] The potential of additional lead electrodes more proximally located on a CS lead with both pacing and sensing characteristics which has been suggested to potentially demonstrate benefit to patients undergoing CRT therapy in the future.[30]

As this analysis was retrospective in nature and did not look at the symptomatic or clinical burden of PAF in these patients, this would need to be substantiated with a controlled randomized clinical trial.

Treatment and management of atrial fibrillation continues to be complex in developing a standard clinical strategy. With the complexities of rate control, pulmonary vein ablation, pharmacologic intervention, pacing therapy, confounded with anti-coagulation, the clinical and healthcare burden of atrial fibrillation on patients and healthcare providers has and will continue to be enormous. A multi-faceted approach utilizing different combinations of therapy and treatments may prove as the only effective options in managing these patients.

Study Limitations:

This evaluation reflects the experience with one center and a limited sample size due to the nature of this patient population. As such, the patient population and indication for implantation may have impacted the data as the percent of ventricular pacing has been reported to impact the atrial arrhythmias.[31]

Conclusions:

Bi-atrial pacing with DAO demonstrated an immediate reduction in percent time in mode switch as well as mode switches per day. A lower total number of days were spent in CAF in the BIA group versus the DAO group, 5.55% vs 14.34% respectively. The lacking of statistical significance may be attributed to either the small sample size in this evaluation or the duration of follow-up not being long enough. In addition, all of these patients had other co-morbidities which may also have impacted the results. As such, this data provides a foundation for a larger, prospective multicenter randomized trial to detail the best combination of therapies to prolong the progression and potentially halt the progression of PAF to AF.

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