The Epidemic of Inadequate Bi-Ventricular Pacing in Patients with Persistent or Permanent Atrial Fibrillation and Its Association with Mortality

Running title: Ousdigian et al.; Impact of AF and Biventricular Pacing on Mortality

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Abstract:

**Background** - We classified patients’ atrial fibrillation (AF), assessed its impact on bi-ventricular pacing (BIVP%), and determined if AF classification or BIVP% independently correlate with mortality in Cardiac Resynchronization Therapy Defibrillator (CRT-D) patients.

**Methods and Results** - CRT-D patients were classified as Permanent (daily mean AF burden ≥23 hours), Persistent (≥7 consecutive days of AF ≥23 hours/day), Paroxysmal (≥1 day with AF ≥6 hours), or No/Little AF (all others) using device-detected AF during the 6 months post-implant. We evaluated subsequent all-cause mortality using a multivariable Cox proportional hazards regression. Among 54,019 patients (age 70±11, 73% male, follow-up 2.3±1.2 years), 8% of patients each had Permanent (N=4,449), Persistent (N=4,237), and Paroxysmal AF (N=4,219). A high proportion of patients with Permanent (69%) and Persistent (62%) AF did not achieve high BIVP (>98%). Relative to No/Little AF, patients with AF had increased mortality after adjusting for age, gender, BIVP, and shocks (Permanent: hazard ratio(HR)=1.28 [1.19–1.38], p < 0.001; Persistent: HR=1.51 [1.41–1.61], p < 0.001). Relative to patients with BIVP>98%, patients with reduced BIVP had increased mortality after adjusting for age, gender, AF, and shocks (90-98%: HR=1.20 [1.15-1.26], p<0.001; <90%: HR=1.32 [1.23-1.41], p<0.001). High BIVP% was associated with the greatest mortality improvement in Permanent AF among the AF classifications.

**Conclusions** - High BIVP% wasn’t achieved in two-thirds of 8,686 Persistent or Permanent AF patients and these patients had an increased risk of death. A shift toward more aggressive rate control and/or more pacing may be necessary in patients with AF to maximize the benefits of CRT.

**Key words:** atrial fibrillation, cardiac resynchronization therapy, heart failure, mortality, rate control
Introduction

Cardiac resynchronization therapy defibrillators (CRT-D), have been proven to significantly reduce hospitalizations and all-cause mortality in heart failure patients. Unfortunately, 30-40% of these patients do not realize an improvement in their symptoms and are often referred to as “non-responders”. Rapid conduction of atrial fibrillation (AF) interferes with CRT delivery and has been implicated as a reason for non-response to CRT therapy. Current means of controlling AF in CRT-D recipients, thereby increasing the percentage of bi-ventricular pacing (BIVP), include sinus rhythm management with medications or AF ablation, or controlling the ventricular rate during AF (VRAF) via medications or AV node ablation.

AF is common in heart failure patients with an estimated prevalence of about 5% in those with NYHA Class I to about 50% in those with Class IV symptoms. The majority of studies looking at AF in heart failure patients have suffered from small sample sizes or highly variable assessments of AF burden which can lead to a potential sampling bias and imprecise reporting of AF.

In addition, studies have consistently shown that increased BIVP is associated with better clinical outcomes. Koplan et al. reported reduced mortality in patients who had greater than 92% BIVP. A more recent report from Hayes et al. suggests that the goal for BIVP should be as close to 100% as possible since the lowest mortality risk was found in patients with greater than 98% BIVP. However, neither study utilized a continuous AF detection algorithm, stored daily data on AF and VRAF, categorized the patients by AF classification, or adjusted for shocks.

The de-identified Discovery Link database overcomes many of the limitations described above by utilizing a continuous AF detection algorithm with high accuracy and storing data that includes daily measurements of AF burden, VRAF, and BIVP. The aim of our study...
was to determine how device derived AF classification impacts BIVP% and whether AF classification and BIVP% independently predict mortality in CRT-D patients.

**Methods**

**Data Collection**

Data collection from implanted CRT-D devices was obtained through remote telemetry from the patient’s place of residence, permitting frequent and accurate transfer of the stored programmed and diagnostic data to the Medtronic CareLink data server. The de-identified Discovery™ Link database was created from the stored data of devices implanted in the United States. Parameters included in the analysis were: age, gender, device shocks, CRT-D programming, premature ventricular contractions (PVCs), daily device-detected AF cumulative duration (i.e., burden), daily mean VRAF, and BIVP%.

**Study Patients**

We performed a retrospective, observational analysis utilizing the Discovery™ Link database. Patients were included if they had all of the following: CRT-D device with the required monitoring capabilities, a transmission between 3 and 12 months post-implant, an atrial lead for AF diagnostics, and their device appeared to be programmed with intent to achieve BIVP. The latter was defined as pacing RV→LV or LV→RV and A) pacing mode DDD or DDDR with paced AV and sensed AV < 250 ms, or B) pacing mode DDI or DDIR with lower rate ≥ 40 bpm and paced AV < 250 ms, or C) pacing mode VVI or VVIR with lower rate ≥ 40 bpm.

**CRT-D Programming and Diagnostics**

CRT-Ds were programmed at the discretion of the implanting physician. We evaluated programming at the transmission nearest in time to the 6 months post-implant transmission. The
frequency of remote CRT-D data transmissions was determined by clinicians and patients. All devices recorded the total time spent in AF each day along with the mean VRAF on days when AF was present. Throughout the manuscript the term ‘AF’, when used to describe the device diagnostics, includes any atrial tachyarrhythmias when the A-V pattern was >1:1 for ≥ 32 ventricular events and the median atrial rate was fast (nominally > 171 bpm). Using device stored EGMs and Holter monitor recordings, the AF detection algorithm has been previously shown to have 100% sensitivity for identification of AF duration with a specificity of 99.99% for detecting non-AT/AF rhythms. Similar to the intent of the AF guidelines, we categorized patients based on AF diagnostics as having Permanent AF if the mean daily AF burden was ≥ 23 hours over the entire evaluation period, Persistent AF if there was at least 7 consecutive days of AF ≥ 23 hours/day, or Paroxysmal AF if there was at least one day with AF ≥ 6 hours. All other patients were classified as having No/Little AF.

The BIVP% was calculated from the ventricular pacing and sensing histograms. We divided the BIVP% data into 3 groups using an upper threshold of 98% because that identified a significant change in mortality in prior work and a lower threshold of 90% was chosen because that is the threshold of a notification in the devices used in this study. Therefore the three BIVP groups were: High BIVP (>98%), Moderate (90-98%), and Low (<90%).

PVCs were recorded by the devices and the average number of PVCs per hour was computed. A PVC was defined as a sensed ventricular event that directly follows any other ventricular event with no atrial event between them and the period of the ventricular event was less than 69% of the mean of the last 4 ventricular events.

**Statistical Analysis**

We sought to understand if AF classification and BIVP% in the period prior to 6 months post-
implant correlated with subsequent mortality (Figure 1). Mortality data were obtained by cross-referencing the Social Security Death Index with the device registry. The data were censored 6 months prior to freezing the database to allow adequate time for death reporting.

Kaplan-Meier methods were used to analyze mortality. A multivariable Cox proportional hazards regression model was used to adjust for AF classification and BIVP%, and for the following variables that were chosen \textit{a priori}: gender, age, and presence of any ICD shock. Proportions were compared with the chi-squared test. Chi-squared test was also used for the categorical variables in Table 1 and Kruskal-Wallis was used for continuous variables. An analysis of variance was used for comparisons in Figure 2. P-values < 0.05 were considered statistically significant. Statistical software from SAS, Inc (Version 9.2) was used.

Results

Patients

Overall there were 61,135 patients with adequate data and intent to BIVP. Of those, 7,116 were excluded due to the lack of an atrial lead, resulting in 54,019 patients from over 2,645 centers in the United States being included in this analysis. Patients had an average follow-up of 2.3±1.2 years from the date of implant resulting in a total of 124,497 patient-years of follow-up. The patients were predominantly male (73%) and had an average age of 70±11 years at baseline (Table 1).

AF, VRAF, and Shocks

Approximately one-quarter (24%) of the 54,019 patients had at least one day with ≥ 6 hours of AF during the initial 6 month diagnostic evaluation phase including 8% each in the Paroxysmal, Persistent, and Permanent classifications (Table 1). These AF patients were significantly older and higher proportions were male. The Permanent AF patients were more likely to be
programmed to a non-tracking mode (DDI/R or VVI/R) with higher lower rates near the 6 month transmission.

The daily AF burden during the initial 6 months was dramatically different between the four AF groups ranging from a median of 0.0 hours/day in the No/Little AF to 0.3 hours/day in Paroxysmal AF to 10.4 hours/day in Persistent AF and up to 24 hours/day in Permanent AF. In addition to the 24% of all patients who had at least one day with ≥ 6 hours of AF in the initial 6 months, 11% developed AF during the remaining follow-up (5.1% Paroxysmal, 5.6% Persistent, and 0.1% Permanent). Therefore, over the entire follow-up of 2.3 years, 35% of the CRT-D patients in this cohort had at least one day with AF ≥ 6 hours. Of the patients who had Paroxysmal AF during the initial 6 months, 28% developed Persistent AF, 2% developed Permanent AF, and 37% returned to No/Little AF post 6 months. Nearly one-third (32%) of the initially Persistent AF patients progressed to Permanent AF, 40% remained Persistent, 10% improved to Paroxysmal, and 19% returned to No/Little AF. The patients with Permanent AF initially continued to have high AF burden and reduced pacing during the remaining follow-up (average burden 23 hours/day and 69% of patients had ≤98% BIVP like in initial period).

The Paroxysmal AF patients had higher VRAF with more variation than the Persistent and Permanent AF patients, although their time in AF was minimal (Figure 2A). The risk of an all-cause shock was highest in Persistent AF patients (14%) compared to each other group (all p < 0.001). Patients with Paroxysmal AF (11%) also had an elevated risk of shock compared to either the No/Little AF (5%) or the Permanent AF (4%) patients (p < 0.001).

**BIVP% by AF Classification**

The BIVP% outside of periods of AF was similarly high in the No/Little AF, Paroxysmal AF, and Persistent AF patients (Figure 2B). Similar to their uncontrolled ventricular rates during AF,
the Paroxysmal AF patients had less BIVP and more variation during the brief periods when they were in AF. Nearly half (47%) of the Persistent AF patients had less than 90% BIVP during AF. The Persistent AF patients’ BIVP dropped an average of 13% (standard deviation 19%) from sinus rhythm to AF. Despite slightly better rate control in the Permanent AF group, nearly a third (31%) had low BIVP during their continuous AF. The reduced pacing during AF had less of an impact on the total BIVP% (in and out of AF) in the Paroxysmal AF patients. The No/Little AF group had 35% of patients without high total BIVP%, compared to 46% of the Paroxysmal AF group, 62% of the Persistent AF group, and 69% of the Permanent AF group. BIVP% decreased inversely proportional to PVC burden in the patients with No/Little AF (BIVP Group: Median PVCs/hour; High: 4; Moderate: 40; Low: 94; p < 0.001).

**Mortality**

Patients with Paroxysmal, Persistent, or Permanent AF an increased rate mortality relative to the No/Little AF group before (Figure 3A) and after adjusting for age, gender, CRT-D shock, and BIVP% (Figure 4). Relative to the No/Little AF group, patients with Paroxysmal AF had a 32% increase in mortality rate (Hazard Ratio (HR) = 1.32, 95% confidence interval (CI): 1.22 – 1.42, p < 0.001) while Persistent AF had a 51% increase in mortality rate (HR = 1.51, CI: 1.41 – 1.61, p < 0.001), and Permanent AF had a 28% increase (HR = 1.28, CI: 1.19 – 1.38, p < 0.001) in the multivariable analysis. All AF groups had increased mortality relative to the No/Little AF group in each of the three BIVP patient groups (p < 0.001).

Patients not receiving high BIVP had an increased mortality rate relative to those with high pacing before (Figure 3B) and after adjusting for AF classification, age, gender, and ICD shock(s) (Figure 4). Relative to patients with high BIVP, patients with moderate (90-98%) BIVP had a 20% increase in mortality rate (HR: 1.20, CI: 1.15 – 1.26, p<0.001) and the patients who
received low (<90%) BIVP had a 32% increase in mortality rate (HR= 1.32, CI: 1.23 – 1.41, p<0.001) in the multivariable analysis. We also assessed which AF classification had the largest mortality increase for the AF sub-group that did not receive high BIVP compared to the AF sub-group with high BIVP. The Permanent AF patients with lower pacing (<98%) had the largest increase in mortality at 3 years compared to the Permanent AF patients high BIVP% (mortality increase for Low BIVP vs. High BIVP: No/Little: 23.8%, Paroxysmal AF: 29.7%, Persistent AF: 19.9%, Permanent AF: 42.0%; p < 0.001).

Discussion

Our study is the first to highlight that two-thirds of CRT-D patients with Persistent or Permanent AF in widespread practice did not receive high BIVP%. Patients with AF or reduced BIVP% had an increased risk of death independent of each other and age, gender, or ICD shocks. Of the four AF classifications, the association between high BIVP% and decreased mortality was greatest in Permanent AF patients, however this group is the least likely to receive high BIVP.

Impact of AF Classification on BIVP%

Our CRT-D recipient cohort had an AF prevalence of 24% during the initial 6 months and 35% over 2.3 years. Persistent and Permanent AF patients who have the highest burden of uncontrolled AF had the highest reduction of total BIVP. A high PVC burden often accounts for these findings in these low AF burden groups and Cheng et al. found non-optimal programming (e.g., Paced or Sensed AV Interval) also resulted in reduced BIVP. These findings further underscore the importance of rigorously following patients and the need for expertise in recognizing various factors that affect CRT delivery.

Impact of AF Classification on Mortality

Our study of 54,019 CRT-D patients found that all three AF groups had an increased risk of
mortality relative to the No/Little AF patients after adjusting for age, gender, CRT-D shocks, and BIVP%. The impact of AF in patients with ICDs/CRT-Ds has been limited by relatively small sample sizes. A study by Santini et al included 122 CRT-D patients with Persistent AF and 33 with Permanent AF. They also found that Persistent or Permanent AF patients had a higher risk of the combined endpoint of heart failure hospitalization or death. Wilton et al. also found that patients with a history of AF had an increased mortality risk relative to the patients without a history of AF in their meta-analysis.

There is a paucity of prospective randomized trials showing CRT-D improves outcomes in AF patients. The CARE-HF trial showed that AF patients had increased mortality compared to patients without AF; however, AF patients who received CRT realized a similar outcomes benefit as the patients without AF who received CRT. The RAFT study stratified Permanent AF patients to ICD (N=115) vs. CRT-D (N=114). They reported that CRT did not improve death or the combined endpoint of death or heart failure hospitalization. RAFT required these patients to have good rate control (≤60 bpm during rest, ≤90 bpm during 6-minute walk test), however, only 34.3% (N = 39 patients) of the permanent AF patients received ≥95% BIVP during the initial 6 months and only one patient received an AV nodal ablation before or within the 6 months after randomization. Two meta-analyses have looked at the impact of CRT in AF patients and both concluded that CRT provides functional improvements or outcomes benefits in AF patients. We also observed lower mortality in patients who received more CRT therapy (i.e., BIVP%) irrespective of their AF classification.

**Impact of BIVP% on Mortality**

Our study found that high (>98%) BIVP% was associated with decreased risk of mortality independent of age, gender, AF classification or ICD shocks. Prior registry and clinical studies
have evaluated BIVP% and found a mortality benefit with higher percentages of BIVP but cut-off values have varied. Koplan et al reported a mortality and heart failure hospitalization benefit with >92% BIVP.\textsuperscript{3} Hayes et al reported an incremental decrease in mortality as the percentage of BIVP increased with greatest benefit observed in patients having greater than 98% pacing.\textsuperscript{6} All of the large studies that have investigated BIVP%, including ours, were limited because they were only able to report device measured BIVP%. These larger studies have not been able to report on effective BIVP capture (i.e., pacing into excitable tissue and thereby avoiding pseudo fusion). In a small study utilizing Holter and device data, Kamath et al showed that effective BIVP capture percent is typically lower than device measured BIVP% in Permanent AF patients and, therefore, is more clinically important (i.e., better predicts CRT response).\textsuperscript{15} The ability to quantify effective BIVP capture (i.e., the quality of CRT) in addition to the BIVP% (i.e., the quantity of CRT) remains an unmet need.

**AF Patients: Significant Opportunity to Improve CRT Efficacy**

The European Heart Rhythm Association and Heart Rhythm Society expert consensus on CRT repeatedly highlights the need to achieve high BIVP%, “as close as possible to 100%,” and that this “is particularly important in patients with AF”.\textsuperscript{16} AV node ablation has risen as an adjunctive therapy such that the expert consensus now recommends: “that it should be considered earlier rather than later during follow-up.” The European Society of Cardiology guidelines note that patients with Permanent AF are considered a class IIa level B only if an AV node ablation is performed so that nearly 100% BIVP can be reached.\textsuperscript{17} Gasparini et al showed that CRT-D patients with Permanent AF who received AV node ablation had significantly lower mortality than the drug-treated AF patients despite these patients receiving >85% BIVP.\textsuperscript{18} Several other studies and meta-analyses have shown benefits including increased ejection fraction, exercise
tolerance, clinical response, and survival.11,19 The BIVP% was high (>98%) in all six of the studies reporting on BIVP% that included patients with AF and an AV node ablation.19 In a more recent multivariable analysis, Gasparini et al found that patients with Permanent AF who were treated with an AV nodal ablation (N=443) had a 52% reduction in mortality compared to Permanent AF patients treated with rate slowing drugs (N=895).20 The Permanent AF patients with AV nodal ablation also had similar mortality to sinus rhythm patients (N=6,046).

Device BIVP% counters are the most optimistic report on pacing therapy yet two-thirds of Persistent or Permanent AF patients are still not receiving high BIVP%. Our study cannot report on the use of medications or ablations but it is obvious that the majority of Persistent and Permanent AF patients are not receiving sufficient rate control to achieve the goal of high BIVP. There are thousands of patients with years of AF and reduced BIVP in widespread practice. Gasparini and Borianni pointed out that studies like the RAFT sub-analysis of Permanent AF patients ‘may be misleading and create confusion’ about the true benefit of CRT in AF patients because the BIVP% was not high.21 Likewise, Persistent and Permanent AF patients in widespread practice are likely not reaping the outcomes benefits that CRT can provide.

Limitations
Our study is a retrospective analysis of prospectively collected data looking at mortality with respect to AF classification and BIVP. Lack of complete clinical data may limit interpretation of our mortality results. The absence of information regarding ejection fraction, heart failure status, medication use, or the use of procedures like ablations or other clinical factors precludes analysis of these variables and their relationship to mortality. Nevertheless, given the size of our cohort and the fact that most CRT-D patients in the timeframe of our study shared a set of similar characteristics based on their indication for a CRT-D device (Ejection Fraction ≤ 35%, wider
QRS, class III - IV heart failure symptoms, and optimal medical therapy), these are important
findings that reflect the real world experience.

By excluding patients without an atrial lead, we may have excluded a portion of
Persistent or Permanent AF patients with CRT-D’s in whom atrial leads aren’t typically
implanted, however, the atrial lead helps provide accurate continuous AF diagnostic information.
Our results are not generalizable to patients without an atrial lead but our study does include
8,686 Persistent or Permanent AF patients which are more than all prior studies and meta-
analyses.

The devices in this study used an algorithm that does not distinguish between atrial
fibrillation and other rapid >1:1 atrial tachyarrhythmias (e.g., atrial flutter) therefore the patients
may have these rhythms included in their ‘AF’ durations.

Lastly, in this analysis, one has to keep in mind that the device measured BIVP% may
overestimate the actual effective BIVP%, especially in patients with AF.

Conclusions
Rate control and/or programming were inadequate to achieve high BIVP% in two-thirds of
Persistent or Permanent AF patients. Patients with AF or reduced BIVP% were associated with
an increased risk of death independent of each other and age, gender, or ICD shocks. Delivering
high BIVP was associated with the greatest mortality benefit in patients with Permanent AF. Our
findings suggest that in widespread practice there is a lack of adherence to following the expert
consensus statements and guidelines for BIVP in patients with Persistent or Permanent AF. A
systematic shift toward more aggressive rate control and/or more pacing may be necessary in
patients with AF to maximize the benefits of CRT.
**Funding Source:** This study was funded by Medtronic, Inc., Minneapolis, Minnesota

**Conflict of Interest Disclosures:** Kevin Ousdigian, Jodi Koehler, and Paul Ziegler are employees of Medtronic, Inc. Dr. Borek has no conflict of interest disclosures. Dr. Heywood has received lecture honoraria, fellowship, and research support from St Jude and lecture honoraria, research support, and has consulted for Medtronic. Dr. Wilkoff is on the Physician Advisory Board for Medtronic, St. Jude, and Spectranetics.

**References:**


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Table 1: Patient Characteristics and CRT-D Programming by AF Classification

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>No/Little AF</th>
<th>Paroxysmal AF</th>
<th>Persistent AF</th>
<th>Permanent AF</th>
<th>P-value across 4 groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Patients (N)</td>
<td>100% (54,019)</td>
<td>76% (41,114)</td>
<td>8% (4,219)</td>
<td>8% (4,237)</td>
<td>8% (4,449)</td>
<td></td>
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<tr>
<td>Mean Follow-up in years (SD)</td>
<td>2.3 (1.2)</td>
<td>2.3 (1.2)</td>
<td>2.3 (1.2)</td>
<td>2.2 (1.2)</td>
<td>2.2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Mean Age in years (SD)</td>
<td>70 (11)</td>
<td>69 (11)</td>
<td>72 (10)</td>
<td>73 (10)</td>
<td>74 (9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male Gender</td>
<td>73%</td>
<td>70%</td>
<td>78%</td>
<td>83%</td>
<td>83%</td>
<td>&lt;0.001</td>
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<tr>
<td>Median AF Hours per day (25th, 75th percentile)</td>
<td>NA</td>
<td>0.0</td>
<td>0.3</td>
<td>10.4</td>
<td>24</td>
<td></td>
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<tr>
<td>ICD Shock(s) during evaluation period</td>
<td>6%</td>
<td>5%</td>
<td>11%</td>
<td>14%</td>
<td>4%</td>
<td>&lt;0.001</td>
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<td>Pacing Mode and Lower Rate DDD/DDDR</td>
<td>65%</td>
<td>73.3%</td>
<td>56%</td>
<td>38%</td>
<td>18%</td>
<td></td>
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<tr>
<td>≤ 60 bpm</td>
<td>23%</td>
<td>21.0%</td>
<td>30%</td>
<td>37%</td>
<td>23%</td>
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<td>70 bpm</td>
<td>6%</td>
<td>4.4%</td>
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<td></td>
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<tr>
<td>VVI/VVIR or DDI/DDIR</td>
<td>2%</td>
<td>0.4%</td>
<td>1%</td>
<td>3%</td>
<td>12%</td>
<td></td>
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<tr>
<td>≤ 60 bpm</td>
<td>3%</td>
<td>0.6%</td>
<td>3%</td>
<td>6%</td>
<td>27%</td>
<td></td>
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<tr>
<td>70 bpm</td>
<td>1%</td>
<td>0.3%</td>
<td>1%</td>
<td>3%</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>≥ 75 bpm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sensed AV (ms)</td>
<td>6%</td>
<td>7%</td>
<td>5%</td>
<td>3%</td>
<td>2%</td>
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<tr>
<td>30-90</td>
<td>64%</td>
<td>63%</td>
<td>61%</td>
<td>67%</td>
<td>76%</td>
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<td>100</td>
<td>30%</td>
<td>30%</td>
<td>34%</td>
<td>30%</td>
<td>22%</td>
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<tr>
<td>Paced AV (ms)</td>
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<td></td>
<td></td>
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<tr>
<td>30 - 120</td>
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<td>9%</td>
<td>8%</td>
<td>6%</td>
<td>5%</td>
<td></td>
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<tr>
<td>130</td>
<td>61%</td>
<td>60%</td>
<td>57%</td>
<td>63%</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>140-240</td>
<td>31%</td>
<td>31%</td>
<td>35%</td>
<td>31%</td>
<td>23%</td>
<td></td>
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<tr>
<td>Conducted AF Response On</td>
<td>95%</td>
<td>95%</td>
<td>94%</td>
<td>94%</td>
<td>92%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Figure Legends:

**Figure 1**: Study Design Model – AF, VRAF, and BIVP% were assessed during the 6 months following implant and then mortality was assessed.

**Figure 2**: Impact of AF Classification on Ventricular Rates and BIVP% - A) Ventricular Rate during AF, B) BIVP%. The AF Burden over the initial 6 months; AF Group: Median (25th-75th%) AF hours per day; No/Little AF Group: 0.0 (0.0 – 0.0) hrs/day, Paroxysmal AF Group: 0.3 (0.1 – 1.0) hrs/day, Persistent AF Group: 10.4 (5.0 – 17.8) hrs/day, Permanent AF: 24 (24 – 24) hrs/day.

**Figure 3**: Unadjusted Mortality - A) AF Classification Groups, B) BIVP% Groups

**Figure 4**: Adjusted Mortality Hazard Ratios for Multivariable Analysis—Hazard Ratios adjusted for age, gender, AF, BIVP%, and Shock(s).
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