Title: Ampere Hour (Ah) as a Predictor of Cardiac Resynchronization Defibrillator Pulse Generator Battery Longevity; A Multi-Center Study.

Running Head : Ampere hour (Ah) predicts CRT-D device longevity.

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Conflict of Interest Related to this Manuscript:

Christopher R. Ellis, MD, FHRS has received consulting fees and advisory board (<$10,000 per year) from Medtronic, Boston Scientific; received significant research funding for investigator initiated studies (paid to Vanderbilt University) from, Boston Scientific, Medtronic.

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Battery Longevity Analysis (Subjects with follow-up time available only)

Abstract:

Background: CRT-D devices improve survival for NYHA II-IV systolic heart failure patients with QRS >120ms and LVEF <35%. A limitation of 100% CRT pacing is excess battery depletion and pulse generator (PG) replacement compared to VVI or dual chamber systems. Ampere-hour (Ah) measures PG battery capacity and may predict CRT-D device longevity.

Methods: We performed a multi-center retrospective study of all CRT-D devices implanted at our centers from August 1, 2008 to December 31, 2010. Analysis was performed for survival to elective replacement indicator (ERI) between 1.0 Ah, 1.4 Ah, and 2.0 Ah devices, per manufacturers specifications.

Results:

1302 patients were studied through December 31, 2014. Patients were followed an average of 3.0 ± 1.3 years (794 1.0 Ah, 322 2.0 Ah, and 186 1.4 Ah devices under study). CRT-D generator ERI occurred in 13.5% of 1.0 Ah systems (107/794), versus 3.8% in 1.4 Ah, (7/186), and 0.3% in 2.0 Ah devices (1/322) over mean follow up of 3.0 yrs. Odds ratio (OR) for reaching ERI with 1.0 Ah device versus 1.4 Ah or 2.0 Ah was 9.73, p <0.0001. Univariate predictors for ERI included 1.0 Ah device and LV pacing output > 3V @ 1 ms (OR 3.74, p<0.001). LV impedance >1000 ohms predicted improved device survival (OR 0.38, p 0.0025).

Conclusions:

CRT-D battery capacity measured by Ampere hour (Ah) is a strong predictor of survival to ERI for modern systems. Further study on cost and morbidity associated with early pulse generator change in 1.0 Ah systems is warranted.

Key words: defibrillator, resynchronization, ICD, battery, longevity, Ampere hour

Abbreviations list:

CRT-D (cardiac resynchronization defibrillator), ICD (implantable cardioverter defibrillator), PG (pulse generator), ERI (elective replacement indicator), Ah (ampere hour), OOS (out of service), CIED (cardiac implantable electronic device), OR (odds ratio)

Manuscript Text:

Introduction:

Cardiac resynchronization (CRT) pacing improves survival, reduces heart failure hospitalization, and lessens ventricular arrhythmia burden in properly selected chronic systolic heart failure recipients[1-3]. Response to CRT is greatest for defibrillator patients with left bundle branch block and QRS duration >150ms with LVEF <35%, and placing the LV lead at the site of latest LV activation provides the best hemodynamic response to CRT[4]. The goal of CRT programming typically is 100% biventricular pacing, which accelerates pulse generator (PG) battery depletion by engaging a third pacing circuit with continuous battery drain, often at higher output. The most common reason a cardiac resynchronization defibrillator (CRT-D) system requires repeat surgical intervention, is for replacement of the pulse generator (PG), which is associated with at least a 4-18% complication rate[5]. The average survival of a CRT-D patient is now 7 years, and in several previously published studies, the survival of a CRT-D pulse generator is at best 50%, 4 years from implant[6,7]. All prior studies on implanted cardioverter defibrillator (ICD) battery longevity have demonstrated a shortened lifespan for CRT systems compared with single (VVI) or dual chamber ICD's, and suggest the majority of CRT-D recipients will need a device generator replacement prior to death, device related infection, or heart transplantation[8,9].

Battery Longevity Analysis (Subjects with follow-up time available only)

Excess battery drain on a CRT pulse generator may be accelerated by high LV pacing output (typically when >3 Volts @ 1ms), a high percentage of atrial pacing (increased low rate limit, or sinus node dysfunction), and by frequent capacitor discharges for ICD shocks. Ampere hour (Ah) is a measure of remaining battery capacity in the pulse generator and could be a powerful predictor of the survival of the CRT-D device to elective replacement indicator (ERI). We have observed improved device survival for modern CRT-D systems with a 2.0 Ah battery and MnO_2 (Manganese dioxide) cathode versus 1.0 Ah devices at our centers. We hypothesized that CRT-D device survival to ERI would best be predicted by the battery capacity (Ah) of the system at implant.

Methods:

We performed a multi-center retrospective study of all CRT-D devices implanted at our centers from August 1, 2008 to December 31, 2010. All device implant data was confirmed with the CRT-D manufacturers, including patients who had transferred long-term follow up to another center. Demographic variables, device implant data, follow up remote and in-office interrogations were reviewed and entered into the Vanderbilt REDCAP online database by the study investigators. All patient identifiers were removed upon entry into REDCAP and the study underwent complete IRB review and approval at all participating sites. CRT-D survival was calculated from implant date to time of PG replacement, heart transplant, device infection (system extraction), patient death, or the end of the study period. Final data entry allowed was December 31, 2014 at which point the REDCAP database was locked for analysis.

Statistical analysis:

Battery Longevity Analysis (Subjects with follow-up time available only)

Analysis was performed between 1.0 Ah (Medtronic Inc., Minneapolis, MN, USA), 1.4 Ah (St. Jude Medical, St. Paul, MN, USA), and 2.0 Ah (Boston Scientific, Marlborough, MA, USA) devices as defined by manufacturers specifications. Comparison was made between devices for the presence of atrial fibrillation (AF), high LV lead output (>3 Volts @ 1 millisecond), >3 ICD shocks in the lifetime of the device, and % atrial pacing by quartile. Additional comparisons were made for % CRT pacing, RA and RV pacing output, and LV lead impedance. Pacing thresholds, % pacing, low rate limit, and lead impedance values were assessed only with chronic follow up data beyond 3 months post implant, to avoid analysis of acute implant data for device battery depletion. LV lead pacing threshold >3V @ 1ms was chosen as a threshold for high output, as it exceeds the low voltage drain in all devices, requiring an amplifier to achieve the required current output. Data was summarized using summary statistics. Continuous measures were summarized with mean, standard deviation, minimum and maximum. Data were compared across manufacturers using ANOVA. Categorical measures were summarized using counts and percentages, using Chi-Square tests (or Fisher's Exact test) for comparisons across manufacturers.

Additional time-to-event analyses were performed using the Kaplan-Meier method. Estimates and their associated 95% confidence intervals were obtained. Survival was compared across manufacturers via the Log-Rank test. All reported p-values are nominal and no adjustment for multiple comparisons were made. P-values of <0.05 were considered statistically significant. All statistical analyses were performed in SAS Version 9.3 (SAS Institute, Inc., SAS Campus Drive, Cary, NC 27513, USA.). Kaplan-Meier plots were produced using R 3.1.1 (R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org.

Results:

Battery Longevity Analysis (Subjects with follow-up time available only)

A total of 1302 CRT-D devices were implanted between August 1, 2008 and December 31, 2010 at the study centers. The last date of device interrogation follow up data entry was December 31, 2014. The average age at implant was 68.1 ± 11.8 yrs., mean LVEF was 25.1 ± 10.1%, mean QRS duration 152.0 ± 25.6 ms, and 65.1% were NYHA class III.. Patients with a 2.0 Ah device were more likely classified as NYHA class II at baseline (p = 0.002). Complete demographics of the study population and are listed in Table 1, separated by manufacturer. Consistent with previous studies, which demonstrate a male bias in the implantation of ICD systems, 73.0% of subjects were male (p = 0.04). Commensurate with US market share, 61.0% of systems were 1.0 Ah Medtronic devices (794/1302), 24.7% were 2.0 Ah Boston Scientific devices (322/1302) and 14.3% 1.4 Ah St. Jude Medical (186/1302). Reason for CRT-D implantation favored ischemic cardiomyopathy in 56.3%, and non-ischemic cardiomyopathy in 41.9%. There was no difference in indication classification between manufacturers. Category of the device at implant and study entry demonstrated a trend towards more de novo implants with 2.0 Ah devices, and more generator replacements with 1.0 Ah device systems (p=0.053). A fewer number of subjects were pacemaker dependant with 2.0 Ah devices when compared to 1.0 Ah devices (p = 0.029). Pacemaker dependence did not however predict CRT-D reaching ERI. This was likely due to all devices being intentionally programmed with a goal to achieve 100% CRT pacing, regardless of Ah status or manufacturer (overall % CRT pacing in entire study cohort was 94.55 ± 12.82). Reasons for reduced % of CRT pacing were rapidly conducted atrial fibrillation, and high-density ventricular ectopy. The presence of atrial fibrillation was equally distributed with a similar % of 1.0 Ah device patients having a history of either paroxysmal or persistent atrial fibrillation (38.6% 1.0Ah, versus 42.5% 2.0 Ah, and 41.2% in 1.4 Ah devices, p = 0.125). PVC burden data was not analyzed as accurate PVC counts could not be determined in all subjects. Device parameters by manufacturer are listed in Table 2a and 2b.

Reasons for a device reaching out of service (OOS) included patient death (22.6%), CIED infection (1.2%), device revision with removal of CRT-D generator under study (1.1%), and heart transplantation (1.1%). 115/1302 of CRT-D generators under study reached elective replacement indicator by the end of the study period (8.8%). The majority of CRT-D generators under study remained in service as of December 31, 2014 (1187/1302, or 91.2%). Table 3 lists OOS reason for all devices under study, separated by Ah and manufacturer. No device failures were seen in this study, and all devices reaching ERI did so gradually from expected draw down of baseline capacity. The mean duration of follow up under study did not differ between manufacturers.

Device based predictors of a CRT-D reaching ERI are listed in Tables 4 and 5. The presence of atrial fibrillation and the % of atrial pacing by quartile, did not predict device reaching ERI status (atrial fibrillation OR 1.15, 95% CI 0.78-1.71, p = 0.4712, atrial pacing subgroup analysis <25% versus >75% atrial pacing OR 0.90 95% CI 0.65-1.25, p = 0.5410). The % of CRT pacing compared between <85% CRT pacing, 85-95% CRT pacing and >95% CRT pacing similarly did not predict CRT-D reaching ERI (p = 0.1832). CRT pacing % was not equally distributed between groups (see Table 2a), though the absolute difference in % pacing between 1.0 Ah and 2.0 Ah groups was only 2.64%.

Though ICD shocks and ICD capacitor charges are known to predict early battery depletion, only a limited number of patients (n = 91) had > 3 shocks in the lifetime of the device (defined as high shock burden), compared to low burden (0-1 total shocks). A trend towards reduced CRT-D device survival was seen, but did not meet significance (84.6% device survival in high shock burden group, versus 91.3% device survival in low burden group, p = 0.077). ICD shocks trended towards a higher shock burden in the 2.0 Ah group, but did not met significance (p = 0.288).

The strongest univariate predictor of a device reaching battery depletion for ERI was Ah status or battery capacity. A 1.0 Ah device was significantly more likely to reach ERI status than a 1.4 Ah or 2.0 Ah device, regardless of any additional variable analyzed (OR 9.73 for reaching ERI 1.0 Ah vs 1.4 and 2.0 Ah devices, p <0.0001). Kaplan-Meier analysis of CRT-D device survival is shown in Figure 1. Additional analysis of CRT-D devices reaching ERI was made within each manufacturer. Based on the limited number of 2.0 Ah and 1.4 Ah devices reaching ERI, analysis could only be performed for 1.0 Ah devices. There were 542 Medtronic Consulta, 229 Concerto, 20 Maximo, and 3 Protecta devices under study. There was no difference in device survival between the 1.0 Ah Concerto and 1.0 Ah Consulta models (Log-rank test comparing time to ERI OOS, p=0.3776).

Battery Longevity Analysis (Subjects with follow-up time available only)

Additional predictors of CRT-D battery depletion included low LV lead impedance <500 ohms, compared to LV lead impedance >1000 ohms in chronic follow-up (OR 0.38 for device survival with >1000 ohms vs. <500 ohms, p = 0.0025). Also, LV lead programmed pacing output >3V @ 1ms vs. <3V @ 1ms strongly predicted device survival across all manufacturers (OR 3.74, p<0.001). There were a higher proportion of patients programmed to high LV lead output in the 2.0 Ah cohort (13.8% 2.0 Ah, vs 8.3% in 1.0 Ah cohort, p = 0.025). Kaplan Meier analysis by LV output is presented in Figure 2 and Figure 3. Notably, with 1.0 Ah devices programmed to >3V @ 1ms, nearly all CRT-D device generators reached ERI by 4 years post implant (59/63), suggesting that lower initial battery capacity was heavily impacted by the additional LV lead current drain at high output .

High shock burden, % CRT pacing, LV lead programmed >3V @ 1ms, and LV lead impedance were not equally distributed between Ah groups as previously discussed, due to the non-randomized nature of the study (see Table 2a, 2b and 5). More shocks were delivered, and a higher % of LV leads were programmed >3V @ 1ms in the 2.0Ah group, additionally, the mean LV lead impedance was lower in the 2.0 Ah group. Despite these factors known to deplete an ICD generator, 2.0 Ah devices remained significantly more likely to remain in service. Regarding additional pacing co-variates, there was no effect of RA or RV pacing threshold as a univariate predictor of a device reaching ERI, despite small but significant differences between manufacturers. The vast majority of devices in this study were programmed 2.0V @ 0.4ms on both RA and RV leads. Similarly, RA and RV lead impedance were not found to predict CRT-D device survival despite similar small differences in mean impedance value (see Table 2b).

Discussion:

Battery Longevity Analysis (Subjects with follow-up time available only)

Our multi-center study on CRT-D device longevity demonstrated a strong inverse relation between pulse generator capacity (Ah) and battery depletion for modern CRT-D devices. Battery chemistry and the demands of a CRT-D system have evolved dramatically from the initial low current Ni+-Cadmium and Zn2+-Mercury cells of original pacemakers in the 1950's. Lithium-iodide batteries have been the mainstay of low power systems (pacing output in the milli Amp range) since about 1973, but with ICD systems, the ability to charge a capacitor to over 800V, requires higher current drain on the battery, often on the order of 10-20 Amp. CRT-D batteries were initially outsourced by manufacturers, but several device companies have taken over battery design and manufacturing in house. Changing from Li+-DSVO to Li+-MnO2 chemistry, and reconfiguring the limited available space within the CRT-D generator 'can', Boston Scientific Inc., produces a 2.0 Ah rating assessed by charge metering on their current CRT-D pulse generators utilizing a MnO2 (Manganese dioxide) cathode. This appears to have significantly impacted CRT-D device survival to ERI in our practice, forming the hypothesis for this study.

Previous multi-center studies on battery longevity of ICD systems did not focus on CRT systems alone, and as such, have less ability to differentiate the effect of battery chemistry or Ah capacity alone on CRT-D device survival[6,7]. One would expect to see the impact of changes in battery chemistry or capacity on longevity in the highest use device (CRT-D), given both a goal of 100% biventricular pacing, and potential capacitor charges for ICD shocks. All prior ICD longevity studies, which included CRT-D systems, do show that CRT devices have significantly reduced survival compared with ICD's programmed VVI or DDD with RV only pacing. In the Schaer et al., and Thijssen et al., studies, battery capacity between 1.0, 1.1-1.45 and >1.45 Ah devices did not predict a device reaching ERI. However there were no devices with 2.0 Ah battery capacity and an MnO2 cathode under study. The survival curves of both 1.0 Ah and 1.4 Ah devices in our study, match closely the survival curves for CRT-D systems in the previously references longevity studies. However, the device survival curve to ERI for a 2.0 Ah device with MnO2 cathode appears to be on a significantly delayed trajectory in our study.

Battery Longevity Analysis (Subjects with follow-up time available only)

A recently published single-center retrospective study from University of Pittsburgh, demonstrated survival differences in CRT-D generators comparable to our findings (improved survival of Boston Scientific devices compared with Medtronic). The Alam et al., study included many Boston Scientific devices with outsourced non-MnO2 batteries held over from Guidant devices, with 1.0-1.4 Ah battery capacity. These devices are no longer commercially available[11].

The Kaplan-Meier survival curves (Figure 1) of CRT-D to ERI in our study based on Ampere hour (Ah), suggest that CRT systems with 2.0 Ah battery capacity outlast 1.4Ah or 1.0 Ah battery capacity devices with comparable programmed device parameters comparable to the recently published study by Landolina et al[12]. When analyzing devices programmed specifically to high use conditions (i.e., LV lead programmed output >3V @ 1ms, low LV lead impedance <500 ohms, or high shock burden >3 shocks in device lifetime), the survival differences between the Ah groups were magnified in our study.

In keeping with other recent studies reporting beneficial effects of CRT on reduced ventricular arrhythmia (VT/VF) burden, we saw a very low rate of ICD shocks or ATP therapy delivered in over 1200 patients followed for 3 years[2,3]. Analysis of the high use condition of >3 shocks per CRT-D device lifetime trended towards significance in our study (84.6% device survival in high shock burden group, versus 91.3% device survival in low burden group, p = 0.077). However, the limited number of subjects with >3 shocks in the 2.0 Ah group precluded any valid conclusion of this effect on device survival in a multi-variate model.

Additional factors that may accelerate battery drain include low LV pacing impedance increasing current drain, RA and RV pacing output, and low rate limit pacing set at 70 or 80 bpm, rather than allowing preferential atrial sensing. In our study, low LV lead impedance predicted CRT-D reaching ERI when compared to LV impedance >1000 ohms. Quadripolar pacing leads became available during the study, and could have allowed more options to select LV pacing vectors that reduced PG battery drain (favoring high LV impedance and low LV programmed pacing output)[13]. We did not analyze quadripolar LV lead model versus bipolar, but a comparison between unipolar and bipolar LV pacing demonstrated no difference in device survival to ERI. Regarding parameters on the RA and RV leads, there was no effect of RA or RV pacing output or RA or RV lead impedance as a univariate predictor of a device reaching ERI, despite small but significant differences between manufacturers. The vast majority of devices in this study were programmed 2.0V @ 0.4ms on both the RA and RV leads. The small difference in mean pacing voltage would not be expected to account for the survival to ERI differences observed. One recent device feature in 1.0 Ah devices that was not accounted for in our study is the ability to provide LV only pacing (Adaptive CRT).

In summary, CRT-D device longevity can be impacted by the device specifications (battery capacity and chemistry), the programmed parameters of the device, and patient factors such as intrinsic heart rate and VT/VF burden. Reducing the number of CRT-D device generator changes by prolonging device survival is appealing to both patients, and the health care system, as a means to reduced overall cost burden, and fewer device related complications for elective replacement of the ICD generator. Overall, the strongest single predictor of a CRT-D reaching elective replacement for battery depletion in our study was low Ah (1.0 Ah) device status vs 1.4 or 2.0 Ah device, with an OR of 9.73, P <0.0001. Selecting LV pacing vectors to maximize LV pacing impedance (>1000 ohms) and to keep LV output <3V @ 1ms would also be expected to significantly improve CRT-D device survival.

Study limitations: This study was retrospective and as such is subject to selection bias as it was non-randomized. To minimize interpretation bias, statistical analysis was performed off site with a third party statistician. There were no pre-determined methods to adjust for multiple comparisons and caution should be used when interpreting statistical tests. The limited number of ICD shocks and capacitor charges in our cohort prevented the ability to accurately analyze the effects of shocks on battery drain. Based on prior studies the impact of a full capacitor charge on longevity drain is estimated at one month[7].

Due to the modern cohort analyzed, there were no low capacity devices (<2.0 Ah), or 2.0 Ah non-MnO2 devices by Guidant Inc, or Boston Scientific Inc, to make a comparison of the effect of Ah within this manufacturer. Direct comparison between Medtronic 1.0 Ah Consulta and 1.0 Ah Concerto models did not alter survival to ERI. Counter to prior published longitudinal studies[6,7], the % of CRT pacing did not predict CRT-D device survival. This is likely because our study included only CRT systems, and there was no group of VVI or dual chamber ICD's to compare with. All devices under study were intentionally programmed to target >95% CRT pacing, and all prior published studies confirm reduced survival for CRT systems versus VVI or dual chamber devices.

High ICD shock burden >3, LV pacing output >3V @ 1ms, and low LV impedance were more prevalent in 2.0 Ah systems in our study, which should have reduced survival in 2.0 Ah systems. Atrial pacing, and % CRT pacing was highest in the 1.0 Ah group. This is likely a result of the lack of randomization. However, the small absolute increase in CRT pacing % (2.64%) in 1.0 Ah systems would not be expected to make a meaningful impact on overall device longevity. 1.0 Ah Adaptive CRT-D (LV only pacing) was not analyzed, as devices were not commercially available during the study period. This feature may prolong the survival of a 1.0Ah system when able to be utilized. An additional feature that was not analyzed was the use of Auto Capture features to program pacing outputs closer to capture threshold. Previously this has been shown to prolong pacemaker longevity by up to 1-3 years[14].

Conclusions:

In conclusion, battery capacity measured by Ampere hour (Ah) is a useful predictor of survival to ERI for modern CRT-D generators. LV pacing output >3V @ 1ms, low LV lead impedance (<500 ohms) versus high LV impedance (>1000 ohms), and 1.0 Ah versus 1.4 or 2.0 Ah device, predicted early battery depletion in CRT-D systems. Further study is warranted to determine the cost and morbidity associated with earlier CRT-D pulse generator changes in 1.0 Ah systems.

Battery Longevity Analysis (Subjects with follow-up time available only)

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Battery Longevity Analysis (Subjects with follow-up time available only)

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Figure 1. Kaplan-Meier Device Survival to Elective Replacement Indicator (ERI). OOS = Out of Service.

Battery Longevity Analysis (Subjects with follow-up time available only)

Figure 2. Kaplan-Meier Device Survival to Elective Replacement Indicator (ERI) for devices with LV lead programmed output less than 3 Volts @ 1 millisecond.

Figure 3. Kaplan-Meier Device Survival to Elective Replacement Indicator (ERI) for devices with LV lead programmed output greater than 3 Volts @ 1 millisecond.

Table 1. Patient Demographics and CRT-D Implant Data.

Table 2a and 2b. Programmed CRT-D Device Parameters.

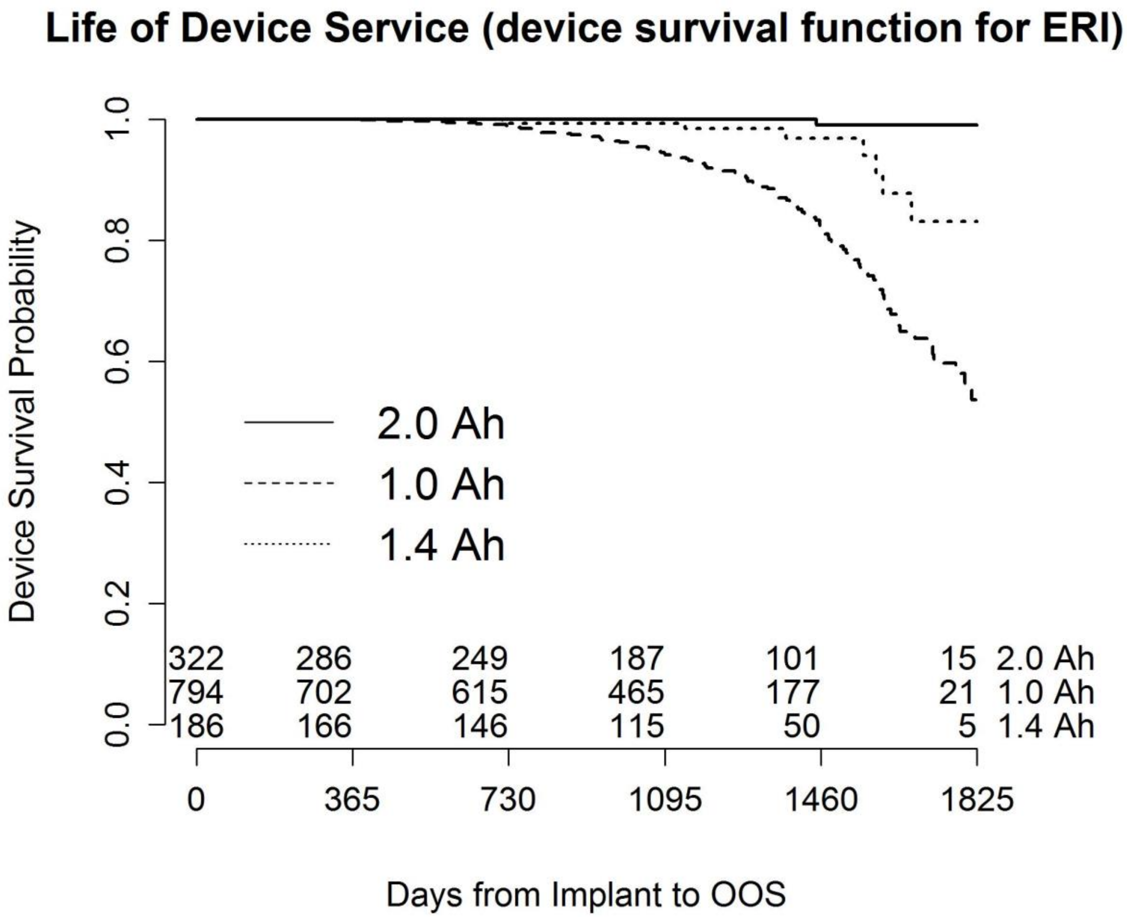
Battery Longevity Analysis (Subjects with follow-up time available only)

Table 3. Device Survival Across Manufacturer, and Out of Service (OOS) Reason.

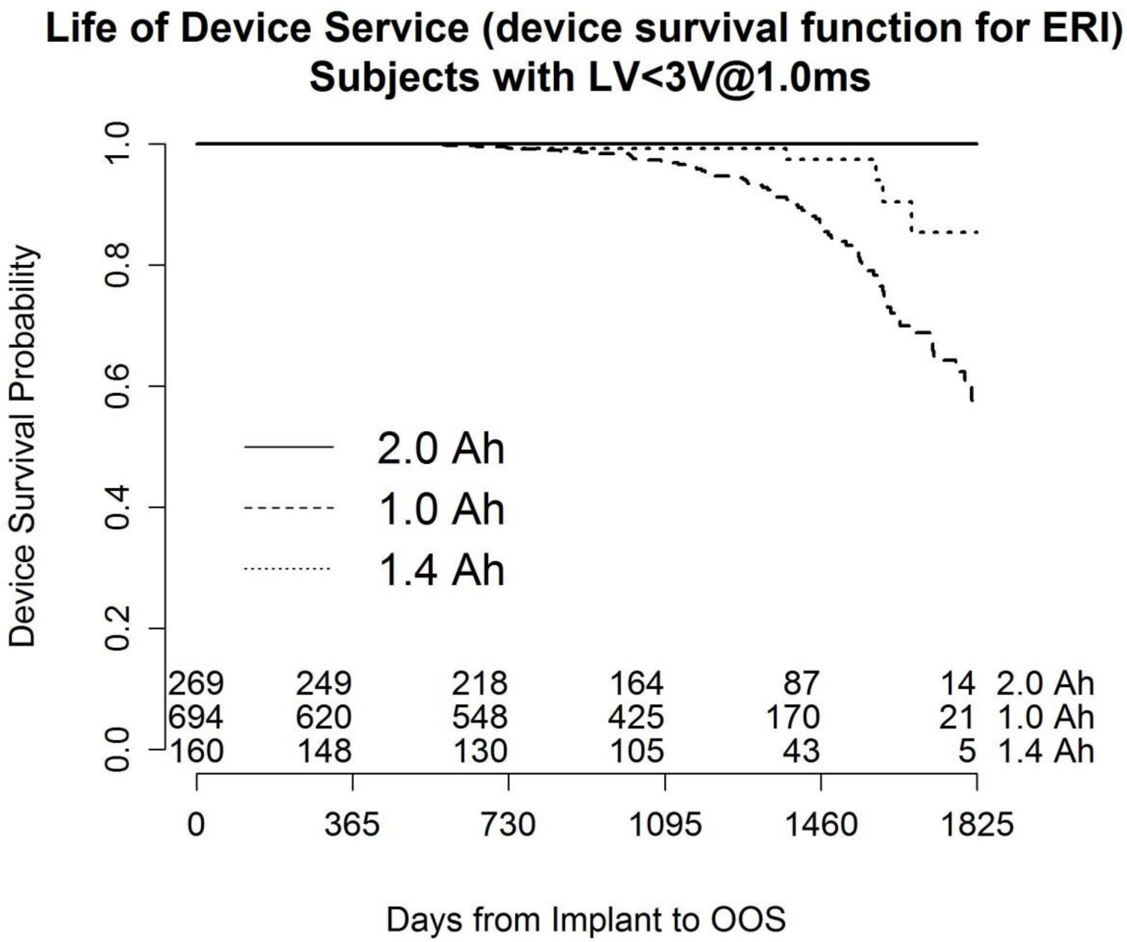
Table 4. Univariate Predictors of a Device Reaching ERI.

Table 5. Additional CRT-D Programming Predictors of ERI.

Battery Longevity Analysis (Subjects with follow-up time available only)



Battery Longevity Analysis (Subjects with follow-up time available only)



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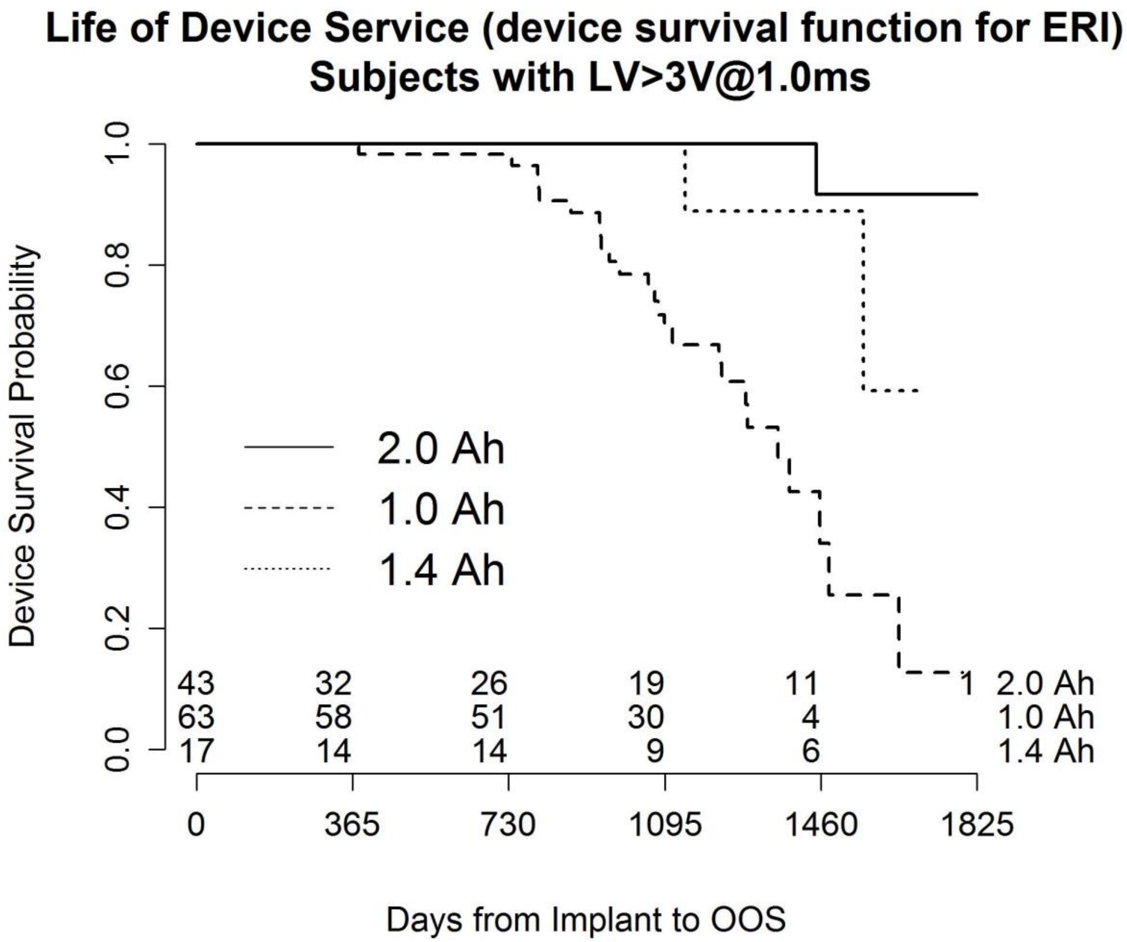

Battery Longevity Analysis (Subjects with follow-up time available only)

Table 1: Patient Demographics and CRT-D Implant Data								
Demographic Data	**Overall (BSC, MDT, SJM)**	**2.0 Ah BSC**	**1.0 Ah MDT**	**1.4 Ah STJ**	**p**	**p 2.0 Ah vs 1.0 Ah**	**p 1.4 Ah vs 1.0 Ah**	**p 2.0 Ah vs 1.0Ah**
Total Enrollment Number	1302	322	794	186				
Gender					0.0395	0.1709	0.0791	0.0109
Male	73.0% (950/1302)	77.0% (248/322)	72.9% (579/794)	66.1% (123/186)				
Female	27.0% (352/1302)	23.0% (74/322)	27.0% (215/794)	33.8% (63/186)				
NYHA Class					0.0002	0.000986	0.0238707	0.1081541
II	28.0% (364/1300)	34.0% (109/321)	26.5% (210/793)	24.2% (45/186)				
III	65.1% (846/1300)	61.4% (197/321)	64.9% (515/793)	72.0% (134/186)				
IV	3.3% (43/1300)	3.7% (12/321)	3.2% (25/793)	3.2% (6/186)				
n/a	3.6% (47/1300)	0.9% (3/321)	5.4% (43/793)	0.5% (1/186)				
Indication					0.2404			
ICM	56.3% (731/1299)	58.8% (188/320)	56.0% (444/793)	53.2% (99/186)				
NICM	41.9% (544/1299)	38.8% (124/320)	42.4% (336/793)	45.2% (84/186)				
VT/VF Arrest	1.4% (18/1299)	1.3% (4/320)	1.4% (11/793)	1.6% (3/186)				
HOCM	0.5% (6/1299)	1.3% (4/320)	0.3% (2/793)	0.0% (0/186)				
Device Category					0.0534			
De novo	38.1% (496/1302)	41.9% (135/322)	35.1% (279/794)	44.1% (82/186)				

Battery Longevity Analysis (Subjects with follow-up time available only)

Table 1: Patient Demographics and CRT-D Implant Data								
Demographic Data	**Overall (BSC, MDT, SJM)**	**2.0 Ah BSC**	**1.0 Ah MDT**	**1.4 Ah STJ**	**p**	**p 2.0 Ah vs 1.0 Ah**	**p 1.4 Ah vs 1.0 Ah**	**p 2.0 Ah vs 1.0Ah**
Replacement	36.9% (480/1302)	33.2% (107/322)	38.5% (306/794)	36.0% (67/186)				
Revision	4.0% (52/1302)	3.7% (12/322)	4.8% (38/794)	1.1% (2/186)				
Upgrade	21.0% (274/1302)	21.1% (68/322)	21.5% (171/794)	18.8% (35/186)				
Pre-implant Intrinsic QRS Duration (MS)	152.0 ± 25.6 (893) 15.0-260.0	152.5 ± 23.7 (220) 92.0-225.0	151.7 ± 26.4 (549) 15.0-260.0	152.3 ± 25.6 (124) 80.0-236.0	0.9171			
100% Paced (pacemaker dependent)					0.0291	0.0090269	0.9437568	0.062037
Yes	25.6% (320/1251)	19.9% (63/316)	27.5% (209/759)	27.3% (48/176)				
No	74.4% (931/1251)	80.1% (253/316)	72.5% (550/759)	72.7% (128/176)				
Atrial Fibrillation					0.1252			
Permanent	15.0% (191/1274)	18.2% (58/318)	13.9% (108/779)	14.1% (25/177)				
Paroxysmal	25.2% (321/1274)	23.0% (73/318)	24.8% (193/779)	31.1% (55/177)				
None	59.8% (762/1274)	58.8% (187/318)	61.4% (478/779)	54.8% (97/177)				
Pre-implant LVEF	25.1 ± 10.1 (1190) 2.0-75.0	24.2 ± 9.8 (295) 5.0-69.0	25.8 ± 10.4 (725) 2.0-75.0	23.4 ± 9.3 (170) 5.0-60.0	0.0041	0.017121	0.4405885	0.0050895
Data summarized as Mean ± SD (N), Min-Max or percent (n/N).								

Battery Longevity Analysis (Subjects with follow-up time available only)

Table 2a: Device Parameters by Manufacturer and Overall

	2.0 Ah (BSC)	**1.0 Ah (MDT)**	**SJM**	**Overall**	**P-value***
LRL (Low Rate Limit)	61.16 ± 8.90	62.38 ± 8.43	62.21 ± 7.26	62.05 ± 8.41	0.0902
LV Impedance	715.88 ± 261.73	606.74 ± 269.51	662.75 ± 249.46	643.94 ± 268.01	0.0003
Atrial Fibrillation at Implant	41.2%	38.6%	45.2%	40.2%	0.1252
Atrial Pacing %	27.32 ± 30.89	35.06 ± 33.63	33.10 ± 34.13	32.80 ± 33.16	0.0056
BiV Pacing	92.83 ± 13.27	95.47 ± 12.44	93.59 ± 13.32	94.55 ± 12.82	0.0051

Table 2b. Programmed Parameters by Manufacturer and Overall

Parameter	Category	Overall	2.0 Ah (BSC)	1.4 Ah (SJM)	1.0 Ah (MDT)	ANOVA P-value
RV Lead Programmed Pacing Voltage	Mean	2.24 ± 0.55	2.37 ± 0.5	2.23 ± 0.58	2.19 ± 0.55	<0.0001
	Median	2.08	2.33	2.08	2.01	
	N	1260	316	177	767	
RA Lead Programmed	Mean	2.07 ± 0.63	2.29 ±0.55	2.12 ± 0.55	1.97 ± 0.66	<0.0001

Battery Longevity Analysis (Subjects with follow-up time available only)

Pacing Voltage						
	Median	2	2.21	2	1.86	
	N	1124	267	160	697	
RA Lead Impedance (Ohms)	Mean	486.2	528.8 ± 35.3	421.4	478.4	<0.001
RV Lead Impedance (Ohms)	Mean	516.6	551.7 ± 113.1	455.6	510.3	<0.001

Table 3. Reason for device Out of Service (OOS)Reason for Out of Service	Overall	2.0 Ah	1.4 Ah	1.0 Ah
Battery Reached ERI	8.8%	0.3%	3.8%	13.5%
	115 / 1302	1 / 322	7 / 186	107 / 794
Patient Death	22.6%	28.0%	16.7%	21.8%
	294 / 1302	90 / 322	31 / 186	173 / 794
Device Revision	1.1%	0.6%	0.5%	1.4%
	14 / 1302	2 / 322	1 / 186	11 / 794
Heart Transplant	1.1%	1.6%	0.5%	1.0%
	14 / 1302	5 / 322	1 / 186	8 / 794

CIED Infection	1.2%	0.9%	0.5%	1.4%
	15 / 1302	3 / 322	1 / 186	11 / 794
Other (Device or Lead Failure)	2.3%	1.2%	1.6%	2.9%
	30 / 1302	4 / 322	3 / 186	23 / 794

Table 4: Univariate Device Parameters as Predictor of ERI OOS

	Odds Ratio*	**95% CI**	**P-value**
Ah by manufacturer (MDT 1.0Ah vs BSC 2.0 Ah and SJM 1.4Ah)	9.73	4.70-20.15	<0.0001
LRL: $^{\beta}$			
<51 vs [51-61)	0.94	0.51-1.72	0.8374
<51 vs [61-71)	0.62	0.33-1.18	0.1426
<51 vs 71+**	0.72	0.47-1.11	0.1358
LV Impedance:$^{\Omega}$			
>1000 vs ≤500	0.38	0.20-0.71	0.0025
>1000 vs (500-700]	1.34	0.66-2.73	0.4199

>1000 vs (700-1000]	0.71	0.35-1.42	0.3275
BiV Pacing: €			
<70 vs [70-80)	0.50	0.04-5.76	0.5782
<70 vs [80-90)	0.36	0.04-3.1	0.3527
<70 vs [90-95)	0.31	0.04-2.45	0.2660
<70 vs [95-100]	0.43	0.08-2.18	0.3067

*Measuring odds of OOS for ERI.

**Note: only 9 subjects had greater than 80 for LRL, and were included in the 71+ category for analysis.

β P-value for any difference across LRL groupings =0.0442

Ω P-value for any difference across LV Impedance groupings =0.0044

¥P-value for any difference across Atrial pacing groupings =0.5269

€ P-value for any difference across BiV pacing groupings =0.5285

Table 5: Additional Programming Predictors of ERI	Overall	2.0 Ah	1.4 Ah	1.0 Ah	p-value**
Presence of Atrial Fibrillation	40.2% 512 / 1274	41.2% 131 / 318	45.2% 80 / 177	38.6% 301 / 779	0.252
LV Threshold >3V@1.0ms	9.9%	13.8%	9.6%	8.3%	0.025

Battery Longevity Analysis (Subjects with follow-up time available only)

		123 / 1246	43 / 312	17 / 177	63 / 757	
High Shock/ATP Burden* (>3 shocks)		19.3%	22.3%	10.5%	19.3%	0.288
		91 / 472	23 / 103	4 / 38	64 / 331	
BiV Pacing Percentage	>95%	75.0%	61.5%	76.0%	80.3%	<0.001
		938 / 1251	193 / 314	133 / 175	612 / 762	
	85-95%	16.0%	27.1%	11.4%	12.5%	
		200 / 1251	85 / 314	20 / 175	95 / 762	
	<85%	9.0%	11.5%	12.6%	7.2%	
		113 / 1251	36 / 314	22 / 175	55 / 762	
Atrial Pacing Percentage	<25%	53.9%	62.0%	54.9%	50.2%	0.010
		570 / 1058	168 / 271	84 / 153	318 / 634	
	25-75%	28.5%	26.2%	27.5%	29.8%	
		302 / 1058	71 / 271	42 / 153	189 / 634	
	>75%	17.6%	11.8%	17.6%	20.0%	
		186 / 1058	32 / 271	27 / 153	127 / 634	

*High='High ATP' burden or >3 total shocks on device; Compared to Low='Low ATP' burden or 0/1 shocks on device.
** p values are for differences between 2.0 Ah, 1.4 Ah and 1.0 Ah groups.

OOS for ERI by subgroup p-values on Overall data, excluding Other (Fisher's exact test):

Atrial Fibrillation Subgroups: Odds Ratio 1.15 (0.78-1.71) p=0.4712 for Atrial Fibrillation Yes vs No
LV subgroups: Odds Ratio for Device Reaching ERI with >3V @1ms threshold versus <3V @ 1ms = 3.74, p <0.001
Atrial pacing subgroups: Odds Ratio 0.90 (0.65-1.25) p=0.5410 for <25% Atrial Pacing versus >75% Atrial Pacing
High Shock Burden subgroups: p=0.0770, for High Shock Burden versus Low Shock Burden (low N in high shock group)T
BiV pacing subgroups: p=0.1832 for <85% BiV pacing versus >95% BiV pacing