Ampere Hour as a Predictor of Cardiac Resynchronization Defibrillator Pulse Generator Battery Longevity: A Multicenter Study

CHRISTOPHER R. ELLIS, M.D.,* DEANNA I. DICKERMAN, B.S.,† JODI M. ORTON, R.N.,* SOHAIL HASSAN, M.D.,‡ ERIC D. GOOD, D.O.,§ TOSHIMASA OKABE, M.D.,¶ JOHN A. ANDRIULLI, D.O.,** KARA J. QUAN, M.D.,†† and ARNOLD J. GREENSPON, M.D.‡‡

From the *Vanderbilt Heart and Vascular Institute, Vanderbilt University Medical Center, Nashville, Tennessee; †Vanderbilt University Medical School, Nashville, Tennessee; ‡Henry Ford Hospital Detroit, Detroit, Michigan; §University of Michigan/Cardiovascular Center, Ann Arbor, Michigan; ¶Thomas Jefferson University, Philadelphia, Pennsylvania; **Cooper Health System, Camden, New Jersey; ††North Ohio Heart Center, Elyria, Ohio; and ‡‡Cardiac Electrophysiology Laboratory, Philadelphia, Pennsylvania

Background: *Cardiac resynchronization defibrillator (CRT-D) devices improve survival for New York Heart Association classes II-IV systolic heart failure patients with QRS > 120 ms and left ventricular ejection fraction < 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 multicenter 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: *One thousand three hundred and two patients were studied through December 31, 2014. Patients were followed for 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 out of 794), versus 3.8% in 1.4 Ah (seven out of 186), and 0.3% in 2.0 Ah devices (one out of 322) over mean follow-up of 3.0 years. 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 >1,000 ohms predicted improved device survival (OR: 0.38, P = 0.0025).*

Conclusions: *CRT-D battery capacity measured by Ah is a strong predictor of survival to ERI for modern systems. Further study on cost and morbidity associated with early PG change in 1.0 Ah systems is warranted. (PACE 2016; 39:658–668)*

defibrillator, resynchronization, ICD, battery, longevity, Ampere hour

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 >150 ms with left ventricular ejection fraction (LVEF) < 35%, and placing the left ventricular (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

Funding sources: Partial funding for this study was provided by Boston Scientific Inc., for IRB review and financial support for independent statistical analysis. Centralized data collection was performed with the Vanderbilt University RED Cap system. Conflicts of Interest: Christopher R. Ellis, M.D., 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. Arnold J. Greenspon, M.D., has consulting fees (<$10,000 per year) and received significant research funding from Boston Scientific, Medtronic. Eric D. Good, D.O., has consulting fees (<$10,000 per year) and received significant research funding from Boston Scientific, Medtronic.

Address for reprints: Christopher R. Ellis, M.D., Vanderbilt Heart and Vascular Institute, Vanderbilt University Medical Center, 5414 Medical Center East 5th Floor, 1211 21st Avenue South, Nashville, TN 37232-8802. Fax: 615-936-1711; e-mail: Christopher.ellis@vanderbilt.edu

Received January 15, 2016; accepted February 8, 2016.

doi: 10.1111/pace.12831

defibrillator (CRT-D) system requires repeat surgical intervention is for replacement of the 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 PG is at best 50%, 4 years from implant.[6,7] All prior studies on implantable cardioverter defibrillator (ICD) battery longevity have demonstrated a shortened lifespan for CRT systems compared with single- (VVI) or dual-chamber ICDs, 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]

Excess battery drain on a CRT PG may be accelerated by high LV pacing output (typically when >3 Volts @ 1 ms), 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 PG 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 multicenter retrospective study of all CRT-D devices implanted at our centers from August 1, 2008 to December 31, 2010. All device implant data were confirmed with the CRT-D manufacturers, including patients who had transferred long-term follow-up to another center. Demographic variables, device implant data, and 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 institutional review board 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

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 ms), >3 ICD shocks in the lifetime of the device, and % atrial pacing by quartile. Additional comparisons were made for % CRT pacing, right atrial and right ventricular 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 postimplant, to avoid analysis of acute implant data for device battery depletion. LV lead pacing threshold >3V @ 1 ms 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 were summarized using summary statistics. Continuous measures were summarized with mean, standard deviation, minimum, and maximum. Data were compared across manufacturers using analysis of variance. Categorical measures were summarized using counts and percentages, using χ^2 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 was made. P-values of <0.05 were considered statistically significant. All statistical analyses were performed in SAS Version 9.3 (SAS Institute, Inc., Cary, NC, USA). Kaplan-Meier plots were produced using R 3.1.1 (R Core Team [2014], R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org).

Results

A total of 1,302 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 years, mean LVEF was 25.1% ± 10.1%, mean QRS duration 152.0 ± 25.6 ms, and 65.1% were New York Heart Association (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 are listed in Table I, 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

Table I.

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	1,302	322	794	186				
Gender					0.0395	0.1709	0.0791	0.0109
Male	73.0% (950/1,302)	77.0% (248/322)	72.9% (579/794)	66.1% (123/186)				
Female	27.0% (352/1,302)	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% (364/1,300)	34.0% (109/321)	26.5% (210/793)	24.2% (45/186)				
III	65.1% (846/1,300)	61.4% (197/321)	64.9% (515/793)	72.0% (134/186)				
IV	3.3% (43/1,300)	3.7% (12/321)	3.2% (25/793)	3.2% (6/186)				
n/a	3.6% (47/1,300)	0.9% (3/321)	5.4% (43/793)	0.5% (1/186)				
Indication					0.2404			
ICM	56.3% (731/1,299)	58.8% (188/320)	56.0% (444/793)	53.2% (99/186)				
NICM	41.9% (544/1,299)	38.8% (124/320)	42.4% (336/793)	45.2% (84/186)				
VT/VF arrest	1.4% (18/1,299)	1.3% (4/320)	1.4% (11/793)	1.6% (3/186)				
HOCM	0.5% (6/1,299)	1.3% (4/320)	0.3% (2/793)	0.0% (0/186)				
Device category					0.0534			
De novo	38.1% (496/1,302)	41.9% (135/322)	35.1% (279/794)	44.1% (82/186)				
Replacement	36.9% (480/1,302)	33.2% (107/322)	38.5% (306/794)	36.0% (67/186)				
Revision	4.0% (52/1,302)	3.7% (12/322)	4.8% (38/794)	1.1% (2/186)				
Upgrade	21.0% (274/1,302)	21.1% (68/322)	21.5% (171/794)	18.8% (35/186)				

(Continued)

Table I.

Continued

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
Preimplant 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% (320/1,251)	19.9% (63/316)	27.5% (209/759)	27.3% (48/176)				
No	74.4% (931/1,251)	80.1% (253/316)	72.5% (550/759)	72.7% (128/176)				
Atrial fibrillation					0.1252			
Permanent	15.0% (191/1,274)	18.2% (58/318)	13.9% (108/779)	14.1% (25/177)				
Paroxysmal	25.2% (321/1,274)	23.0% (73/318)	24.8% (193/779)	31.1% (55/177)				
None	59.8% (762/1,274)	58.8% (187/318)	61.4% (478/779)	54.8% (97/177)				
Preimplant LVEF	25.1 ± 10.1 (1,190) 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 ± standard deviation (N), Min-Max or percent (n/N). Ah = Ampere hour; BSC = Boston Scientific; CRT-D = cardiac resynchronization therapy-defibrillator; HOCM = hypertrophic obstructive cardiomyopathy; ICM = ischemic cardiomyopathy; LVEF = left ventricular ejection fraction; MDT = Medtronic; NICM = nonischemic cardiomyopathy; NYHA = New York Heart Association; SJM = St. Jude Medical; VF = ventricular fibrillation; VT = ventricular tachycardia.

Table II.

Programmed CRT-D Device Parameters

A: 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

B: 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	1,260	316	177	767	
RA lead programmed pacing voltage	Mean	2.07 ± 0.63	2.29 ± 0.55	2.12 ± 0.55	1.97 ± 0.66	<0.0001
	Median	2	2.21	2	1.86	
	N	1,124	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

BiV = biventricular; LV = left ventricular; RA = right atrial; RV = right ventricular. Other abbreviations as in Table I.

1.0 Ah Medtronic devices (794 out of 1,302), 24.7% were 2.0 Ah Boston Scientific devices (322 out of 1,302), and 14.3% 1.4 Ah St. Jude Medical (186 out of 1,302). Reason for CRT-D implantation favored ischemic cardiomyopathy in 56.3%, and nonischemic 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 toward 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-dependent 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 AF and high-density ventricular ectopy. The presence of AF was equally distributed with a similar % of 1.0 Ah device patients having a history of either paroxysmal or persistent AF (38.6% 1.0 Ah, vs 42.5% 2.0 Ah, and 41.2% in 1.4 Ah devices, P = 0.125). Premature ventricular contraction (PVC) burden data were not analyzed as accurate PVC counts could not be determined in all subjects. Device parameters by manufacturer are listed in Table IIA and B.

Reasons for a device reaching out-of-service (OOS) included patient death (22.6%), cardiac implantable electronic device infection (1.2%), device revision with removal of CRT-D generator under study (1.1%), and heart transplantation (1.1%). One hundred and fifteen of 1,302 of CRT-D generators under study reached ERI 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 (1,187 out of 1,302, or 91.2%). Table III 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

Table III.

Device Survival across Manufacturer, and Out-of-Service Reason

	Overall	2.0 Ah	1.4 Ah	1.0 Ah
Battery reached ERI	8.8%	0.3%	3.8%	13.5%
	115/1,302	1/322	7/186	107/794
Patient death	22.6%	28.0%	16.7%	21.8%
	294/1,302	90/322	31/186	173/794
Device revision	1.1%	0.6%	0.5%	1.4%
	14/1,302	2/322	1/186	11/794
Heart transplant	1.1%	1.6%	0.5%	1.0%
	14/1,302	5/322	1/186	8/794
CIED infection	1.2%	0.9%	0.5%	1.4%
	15/1,302	3/322	1/186	11/794
Other (device or lead failure)	2.3%	1.2%	1.6%	2.9%
	30/1,302	4/322	3/186	23/794

Ah = Ampere hour; CIED = cardiac implantable electronic device; ERI = elective replacement indicator.

Table IV.

Univariate Device Parameters as Predictor of ERI OOS

	Odds Ratio†	95% CI	P-Value
Ah by manufacturer (MDT 1.0 Ah vs BSC 2.0 Ah and SJM 1.4 Ah)	9.73	4.70–20.15	<0.0001
LRL:*			
<51 versus (51–61)	0.94	0.51–1.72	0.8374
<51 versus (61–71)	0.62	0.33–1.18	0.1426
<51 versus 71+‡	0.72	0.47–1.11	0.1358
LV Impedance:**			
>1,000 versus ≤500	0.38	0.20–0.71	0.0025
>1,000 versus (500–700)	1.34	0.66–2.73	0.4199
>1,000 versus (700–1,000)	0.71	0.35–1.42	0.3275
BiV pacing:***			
<70 versus (70–80)	0.50	0.04–5.76	0.5782
<70 versus (80–90)	0.36	0.04–3.1	0.3527
<70 versus (90–95)	0.31	0.04–2.45	0.2660
<70 versus (95–100)	0.43	0.08–2.18	0.3067

†Measuring odds of OOS for ERI.
‡Note: only nine subjects had greater than 80 for LRL, and were included in the 71+ category for analysis.
*P-value for any difference across LRL groupings = 0.0442.
**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.
CI = confidence interval; OOS = out-of-service. Other abbreviations as in previous tables.

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 IV and V. The presence of AF and the % of atrial pacing by quartile did not predict device reaching ERI status (AF odds ratio [OR]: 1.15, 95% confidence interval [CI]: 0.78–1.71, P = 0.4712, atrial pacing subgroup analysis <25% vs >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 IIA), though

Table V.

Additional CRT-D Programming Predictors of ERI

		Overall	2.0 Ah	1.4 Ah	1.0 Ah	P-Value**
Presence of atrial fibrillation		40.2%	41.2%	45.2%	38.6%	0.252
		512/1,274	131/318	80/177	301/779	
LV threshold >3 V @ 1.0 ms		9.9%	13.8%	9.6%	8.3%	0.025
		123/1,246	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
		938/1,251	193/314	133/175	612/762	
	85–95%	16.0%	27.1%	11.4%	12.5%	
		200/1,251	85/314	20/175	95/762	
	<85%	9.0%	11.5%	12.6%	7.2%	
		113/1,251	36/314	22/175	55/762	
Atrial pacing percentage	<25%	53.9%	62.0%	54.9%	50.2%	0.010
		570/1,058	168/271	84/153	318/634	
	25–75%	28.5%	26.2%	27.5%	29.8%	
		302/1,058	71/271	42/153	189/634	
	>75%	17.6%	11.8%	17.6%	20.0%	
		186/1,058	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 versus No.
LV subgroups: Odds Ratio for Device Reaching ERI with >3 V @ 1 ms threshold versus <3 V @ 1 ms = 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).
BiV pacing subgroups: P = 0.1832 for <85% BiV pacing versus >95% BiV pacing.
ATP = antitachycardia pacing. Other abbreviations as in previous tables.

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 toward reduced CRT-D device survival was seen, but did not meet significance (84.6% device survival in high shock burden group, vs 91.3% device survival in low burden group, P = 0.077). ICD shocks trended toward a higher shock burden in the 2.0 Ah group, but did not meet 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 three 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).

Additional predictors of CRT-D battery depletion included low LV lead impedance <500 ohms, compared to LV lead impedance >1,000 ohms in chronic follow-up (OR: 0.38 for device survival with >1,000 ohms vs <500 ohms, P = 0.0025). Also, LV lead programmed pacing output >3V @ 1 ms versus <3V @ 1 ms 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 Figures 2 and 3. Notably, with 1.0 Ah devices programmed to >3V @ 1 ms, nearly all CRT-D device generators reached ERI

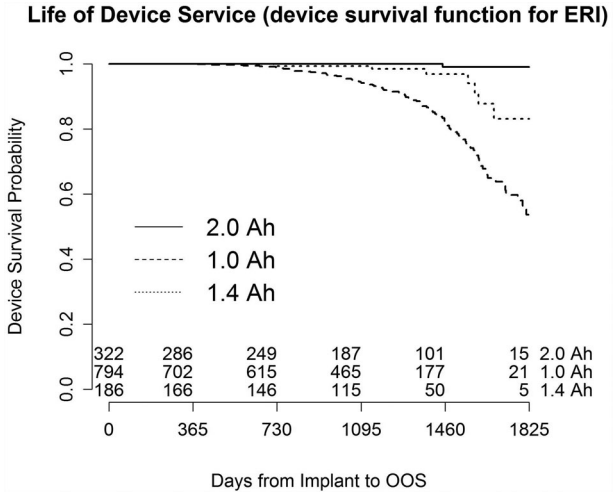

Figure 1. *Kaplan-Meier device survival to elective replacement indicator (ERI). OOS = out-of-service.*

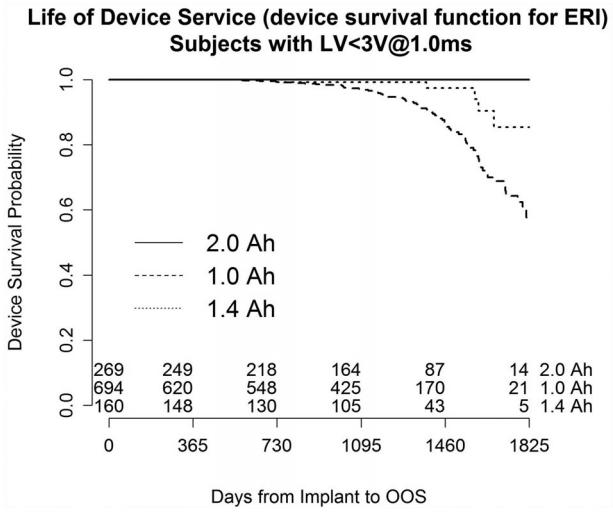

Figure 2. *Kaplan-Meier device survival to elective replacement indicator (ERI) for devices with left ventricular lead programmed output less than 3 V @ 1 ms. OOS = out-of-service.*

by 4 years postimplant (59 out of 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 @ 1 ms, and LV lead impedance were not equally distributed between Ah groups as previously discussed, due to the nonrandomized nature of the study (see Tables IIA/B, IV, and V). More shocks were delivered, and a higher % of LV leads were programmed >3V @ 1 ms in the 2.0Ah group; additionally, the mean LV lead

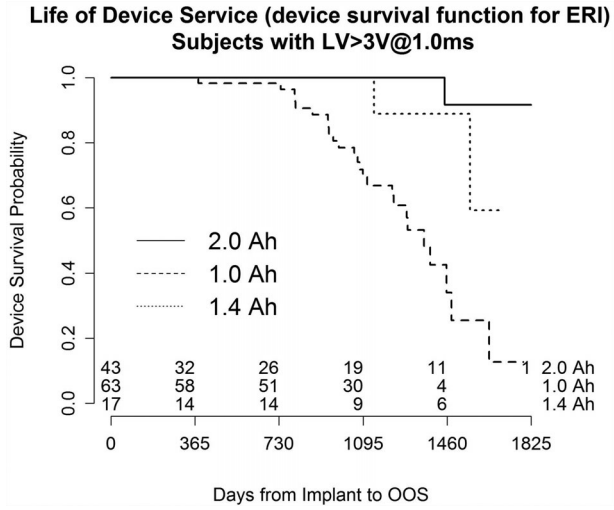

Figure 3. *Kaplan-Meier device survival to elective replacement indicator (ERI) for devices with left ventricular lead programmed output greater than 3 V @ 1 ms.*

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 covariates, 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 @ 0.4 ms 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 IIB).

Discussion

Our multicenter study on CRT-D device longevity demonstrated a strong inverse relation between PG 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 1950s. 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 800 V requires higher current drain on the battery, often on the order of 10–20 Amp.[10] 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+-MnO_2 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 PGs utilizing a MnO_2 cathode. This appears to have significantly impacted CRT-D device survival to ERI in our practice, forming the hypothesis for this study.

Previous multicenter 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 MnO_2 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 referred longevity studies. However, the device survival curve to ERI for a 2.0 Ah device with MnO_2 cathode appears to be on a significantly delayed trajectory in our study.

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-MnO_2 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 (Fig. 1) of CRT-D to ERI in our study based on Ah suggest that CRT systems with 2.0 Ah battery capacity outlast 1.4 Ah 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 @ 1 ms, 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 (ventricular tachycardia (VT)/ventricular fibrillation (VF)) burden, we saw a very low rate of ICD shocks or antitachycardia pacing therapy delivered in over 1,200 patients followed for 3 years.[2,3] Analysis of the high-use condition of >3 shocks per CRT-D device lifetime trended toward significance in our study (84.6% device survival in high shock burden group, vs 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 multivariate 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 beats/min or 80 beats/min, rather than allowing preferential atrial sensing. In our study, low LV lead impedance predicted CRT-D reaching ERI when compared to LV impedance >1,000 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 2.0 V @ 0.4 ms 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 versus 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 (>1,000 ohms) and to keep LV output <3 V @ 1 ms 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 nonrandomized. To minimize interpretation bias, statistical analysis was performed off site with a third party statistician. There were no predetermined 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 1 month.[7]

Due to the modern cohort analyzed, there were no low capacity devices (<2.0 Ah) or 2.0 Ah non-MnO_2 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 ICDs 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 >3 V @ 1 ms, 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. One 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 1.0 Ah 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 Ah is a useful predictor of survival to ERI for modern CRT-D generators. LV pacing output >3 V @ 1 ms, low LV lead impedance (<500 ohms) versus high LV impedance (>1,000 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 PG changes in 1.0 Ah systems.

Acknowledgments: We thank Lisa Thackeray, M.S., Sr. Principal Medical Research Biostatistician @ NAMSA for her help with detailed statistical analysis for this study. Additional study centers we would like to acknowledge include Ashok A. Patel and Subhashini A Gowda at Robert Wood Johnson Health System, New Brunswick, NJ, USA. We would also like to acknowledge Tiffanie M. Markus, PH.D., at Vanderbilt Heart and Vascular Institute who provided real-time database support through REDCap for all study centers.

References

1. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, et al. Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004; 350:2140–2150.
2. Ruwald MH, Solomon SD, Foster E, Kutyifa V, Ruwald AC, Sherazi S, McNitt S, et al. Left ventricular ejection fraction normalization in cardiac resynchronization therapy and risk of ventricular arrhythmias and clinical outcomes: Results from the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT) trial. Circulation 2014; 130: 2278–2286.
3. Stockburger M, Moss AJ, Olshansky B, Klein H, McNitt S, Schuger C, Daubert JP, et al. Time-dependent risk reduction of ventricular tachyarrhythmias in cardiac resynchronization therapy patients: A MADIT-RIT sub-study. Europace 2015; 17: 1085–1091.
4. Derval N, Bordachar P, Lim HS, Sacher F, Ploux S, Laborderie J, Steendijk P, et al. Impact of pacing site on QRS duration and its relationship to hemodynamic response in cardiac resynchronization therapy for congestive heart failure. J Cardiovasc Electrophysiol 2014; 25:1012–1020.
5. Poole JE, Gleva MJ, Mela T, Chung MK, Uslan DZ, Borge R, Gottipaty V, et al. REPLACE Registry Investigators. Complication rates associated with pacemaker or implantable cardioverter-defibrillator generator replacements and upgrade procedures: Results from the REPLACE registry. Circulation 2010; 122:1553–1561.
6. Thijssen J, Borleffs CJ, van Rees JB, Man S, de Bie MK, Venlet J, van der Velde ET, et al. Implantable cardioverter-defibrillator longevity under clinical circumstances: An analysis according to device type, generation, and manufacturer. Heart Rhythm 2012; 9: 513–519.
7. Schaer BA, Koller MT, Sticherling C, Altmann D, Joerg L, Osswald S. Longevity of implantable cardioverter-defibrillators, influencing factors, and comparison to industry-projected longevity. Heart Rhythm 2009; 6:1737–1743.
8. Horlbeck FW, Mellert F, Kreuz J, Nickenig G, Schwab JO. Real-world data on the lifespan of implantable cardioverter-defibrillators depending on manufacturers and the amount of ventricular pacing. J Cardiovasc Electrophysiol 2012; 23: 1336–1342.
9. Biffi M, Ziacchi M, Bertini M, Sangiorgi D, Corsini D, Martignani C, Diemberger I, et al. Longevity of implantable cardioverter-defibrillators: Implications for clinical practice and health care systems. Europace 2008; 10:1288–1295.

10. Root MJ. Implantable cardiac rhythm device batteries. J Cardiovasc Trans Res 2008; 4:254–257.
11. Alam MB, Munir MB, Rattan R, Flanigan S, Adelstein E, Jain S, Saba S. Battery longevity in cardiac resynchronization therapy implantable cardioverter defibrillators. Europace 2014; 16:246–251.
12. Landolina M, Curnis A, Morani G, Vado A, Ammendola E, D'onofrio A, Stabile G, et al. Longevity of implantable cardioverter-defibrillators for cardiac resynchronization therapy in current clinical practice: An analysis according to influencing factors, device generation, and manufacturer. Europace 2015; 17:1251–1258.
13. Forleo GB, Di Biase L, Bharmi R, Dalal N, Panattoni G, Pollastrelli A, Tesauro M, et al. Hospitalization rates and associated cost analysis of cardiac resynchronization therapy with an implantable defibrillator and quadripolar vs. bipolar left ventricular leads: A comparative effectiveness study. Europace 2015; 17: 101–107.
14. Biffi M, Bertini M, Saporito D, Ziacchi M, Stabellini S, Valsecchi S, Ricci V, et al. Automatic management of left ventricular stimulation: Hints for technologic improvement. Pacing Clin Electrophysiol 2009; 32:346–353.