Effect of Continued Cardiac Resynchronization Therapy on Ventricular Arrhythmias After Left Ventricular Assist Device Implantation

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Cardiac resynchronization therapy (CRT) reduces ventricular arrhythmia (VA) burden in some patients with heart failure, but its effect after left ventricular assist device (LVAD) implantation is unknown. We compared VA burden in patients with CRT devices in situ who underwent LVAD implantation and continued CRT (n = 39) to those who had CRT turned off before discharge (n = 26). Implantable cardioverter-defibrillator (ICD) shocks were significantly reduced in patients with continued CRT (1.5 ± 2.7 shocks per patient vs 5.5 ± 9.3 with CRT off, p = 0.014). There was a nonsignificant reduction in cumulative VA episodes per patient with CRT continued at discharge (42 ± 105 VA per patient vs 82 ± 198 with CRT off, p = 0.29). On-treatment analysis by whether CRT was on or off identified a significantly lower burden of VA (17 ± 1 per patient-year CRT on vs 37 ± 1 per patient-year CRT off, p <0.0001) and ICD shocks (1.2 ± 0.3 per patient-year CRT on vs 1.7 ± 0.3 per patient-year CRT off, p = 0.018). In conclusion, continued CRT is associated with significantly reduced ICD shocks and VA burden after LVAD implantation. **(Am J Cardiol 2016;118:556−559)**

Several clinical trials have demonstrated that cardiac resynchronization therapy (CRT) with biventricular pacing improves symptoms, cardiac function, and mortality in patients with heart failure with a reduced ejection fraction and a wide QRS complex.[1−6] CRT appears to reduce the burden of ventricular arrhythmias (VAs) in some subgroups in these studies.[7−12] A small number of patients with chronic heart failure progress to medically refractory disease, requiring durable mechanical cardiovascular support with a continuous flow left ventricular assist device (LVAD). The number of patients implanted with LVADs is increasing,[13] but patients with LVADs were not included in prospective trials of CRT devices. Many patients with LVADs have previously implanted CRT devices, but the effect of continuing CRT in these patients is unknown. We hypothesized that continued CRT would significantly reduce VA burden or appropriate implantable cardioverter-defibrillator (ICD) shocks after LVAD implantation.

Methods

All patients with existing CRT devices implanted with a continuous flow LVAD from January 1, 2007, to December 31, 2012, at a single institution who provided informed consent were included in this study. All data were prospectively collected by regular clinical follow-up at our institution and remote or in-clinic ICD interrogations every 3 months. Patients in whom CRT was continued after discharge after LVAD implantation were included in group 1, and patients in whom CRT was turned off were included in group 2. The decision to turn off CRT was made at the discretion of the treating clinicians. Reasons for turning CRT off included lead malfunction, new onset diaphragm stimulation, battery preservation concerns, and lead extraction because of device infection. Patient demographics, cardiovascular history, laboratory data, ICD interrogations, medication changes, hospitalizations, and device-related surgical interventions were reviewed. VA events were defined as distinct arrhythmia episodes recorded by the ICD within the programmed monitor and therapy zones, excluding nonsustained ventricular tachycardia but including episodes recorded in monitor-only zones and episodes treated by antitachycardia pacing (ATP) or ICD shock. All episodes were confirmed by visual inspection of intracardiac electrograms. Cumulative VA events were defined as the sum of VA events recorded by the ICD between LVAD implantation and termination of data collection at death, heart transplantation, LVAD explantation, or

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This study was conducted at Mayo Clinic Hospital, Phoenix, Arizona. See page 559 for disclosure information.

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Table 1
Baseline characteristics of patients with a cardiac resynchronization therapy (CRT) device in situ undergoing left ventricular assist device (LVAD) implantation

Variable	CRT On (n = 39)	CRT Off (n = 26)	*P* Value
Men	31 (79%)	24 (92%)	0.16
Age at LVAD implantation (years)	62 ± 13	62 ± 14	0.92
Body mass index (kg/m^2)	27 ± 6	28 ± 6	0.49
Ischemic cardiomyopathy	15 (38%)	16 (62%)	0.07
Hypertension	11 (28%)	8 (31%)	0.82
Atrial fibrillation	23 (59%)	19 (73%)	0.24
Diabetes mellitus	15 (38%)	10 (38%)	1.00
Serum creatinine (mg/dL)	1.2 ± 0.4	1.3 ± 0.4	0.46
Serum sodium (mmol/L)	134 ± 5	134 ± 5	0.98
Brain natriuretic peptide (pg/mL)	1233 ± 1056	799 ± 560	0.11
Native QRS duration (ms)	141 ± 27	138 ± 43	0.87
Paced QRS duration (ms)	168 ± 23	164 ± 24	0.44
LV ejection fraction	17% ± 6%	18% ± 6%	0.73
LV end-diastolic dimension (mm)	72 ± 9	71 ± 12	0.87
ICD implanted for primary prevention	33 (85%)	17 (65%)	0.07
Ventricular arrhythmias prior to LVAD	20 (51%)	15 (58%)	0.61
ICD shocks prior to LVAD implantation	16 (41%)	13 (50%)	0.48
Days between ICD and LVAD implantations	718 ± 505	654 ± 617	0.65
Implanted with HeartMate II	34 (87%)	23 (88%)	0.88
LVAD implanted as bridge to transplantation	18 (46%)	8 (31%)	0.21
Antiarrhythmic at discharge	16 (41%)	13 (50%)	0.48
Beta-blocker at discharge	15 (38%)	13 (50%)	0.36

Data expressed as number (%) or mean ± SD.
ICD = implantable cardioverter-defibrillator; LV = left ventricle; LVAD = left ventricular assist device.

completion of the study. VA burden was defined as the mean VA events per patient per year. All ICD programming was at the discretion of the treating clinicians, with the general principals of long VA detection times, high-rate thresholds for device therapies, and several attempts at ATP before ICD shock, strategies that have been associated with improved outcomes.[14,15] This study was performed under an approved institutional review board protocol. Informed consent was obtained from all individual participants included in the study.

Descriptive statistics (including mean and SD for continuous variables and frequency and percentage for categorical variables) were used for demographic data. Two-sample *t* test, one-way analysis of variance, Fisher's exact test, and Pearson chi-square test were used to compare 2 groups when appropriate. Regression analyses with a stepwise elimination approach were used to find predictors for VA after LVAD implantation. Survival curves were constructed by the Kaplan−Meier method and compared by the log-rank test. Any p value <0.05 was considered as statistically significant. Statistical analyses were performed with SAS, version 9.4 software (SAS Institute Inc., Cary, North Carolina).

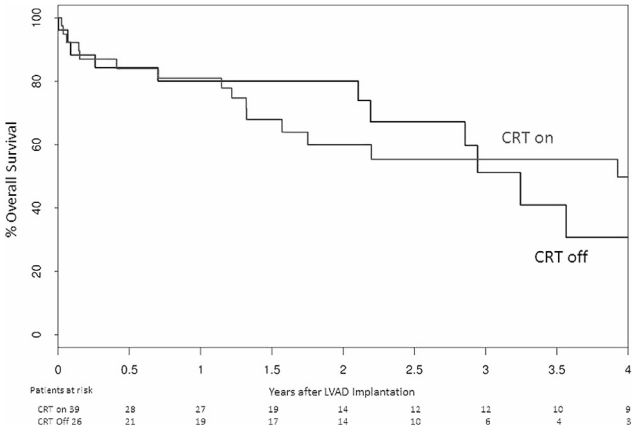

Figure 1. A Kaplan−Meier survival curve comparing survival free of death or heart transplantation in patients whether CRT was continued after discharge, with no significant difference between groups (p = 0.7).

Table 2
Ventricular arrhythmias and subsequent clinical events after left ventricular assist device implantation, analyzed according to whether cardiac resynchronization therapy was continued at discharge or turned off

Variable	CRT On (n = 39)	CRT Off (n = 26)	*P* Value
VA per patient	42 ± 105	82 ± 198	0.29
Total ICD shocks per patient	1.5 ± 2.7	5.5 ± 9.3	0.014
Inappropriate ICD shocks per patient	0.7 ± 2.2	0.6 ± 2.2	0.81
VA treated with antitachycardia pacing per patient	19 ± 64	52 ± 168	0.27
Hospitalizations after LVAD implantation per patient	4.5 ± 4.2	7.6 ± 8.5	0.06
Patients requiring LVAD pump exchanges	8 (21%)	8 (31%)	0.51
ICD pulse generator changes	10 (26%)	11 (42%)	0.29

Data expressed as number (%) or mean ± SD.
ICD = implantable cardioverter-defibrillator; LVAD = left ventricular assist device; VA = ventricular arrhythmia.

Results

HeartMate II (Thoratec, Pleasanton, California) or HeartWare (HeartWare International, Inc., Framingham, Massachusetts) continuous flow LVADs were implanted in 93 patients from January 1, 2007, to December 31, 2012, at our institution. Sixty-five patients (70% of all patients implanted) had functioning CRT defibrillators, and these patients were included in this study. The patients' mean age was 62 years (range 26 to 79 years); 55 (85%) were men, and 31 (48%) had ischemic cardiomyopathy. The indication for ICD implantation was primary prevention in 50 patients (77%); 35 patients (54%) had VA events documented between ICD and LVAD implantation, and 29 (45%) received appropriate ICD shocks before LVAD implantation. The mean time between CRT device implantation to LVAD implantation was 693 ± 549 days (median 576, range 14 to 1,947 days). The indication for LVAD implantation was bridge to transplantation in 26 patients (40%) and destination therapy in 39 patients (60%). After discharge after LVAD implantation, 39 patients (60%) continued CRT and