Impact of Cardiac Resynchronization Therapy on Clinical Outcomes in Patients With Continuous-Flow Left Ventricular Assist Devices

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ABSTRACT

Background: Implantable cardioverter-defibrillators (ICDs) can improve survival in left ventricular assist device (LVAD) recipients. However, the impact of cardiac resynchronization therapy (CRT-D) on outcomes in continuous-flow left ventricular assist device (CF-LVAD) patients is not known. We sought to determine if CRT-D improved clinical outcomes in CF-LVAD patients compared with ICDs alone.

Methods and Results: Sixty-one consecutive CF-LVAD patients with an ICD or CRT-D were evaluated. Impacts of CRT-D on mortality, all-cause hospitalization, and incidence of atrial (AA) and ventricular (VA) arrhythmias after LVAD implantation was compared with patients with ICD alone. Of the 61 LVAD patients, 31 (age 59.8 ± 16 years, 84% male) had CRT-D and 30 (age 57.2 ± 13 years, 74% male) had ICD. Before LVAD implantation, no significant differences were noted between the groups in demographic and clinical characteristics, LVAD indications, and incidence of AA and VA. Over 682 ± 45 days of LVAD support, 8 patients (25.8%) died in the CRT-D arm versus 5 (16.7%) in the ICD arm ($P = .35$). No differences were noted between the CRT-D and ICD groups in all-cause (96.8 vs 93.3%; $P = .63$) and HF (19.4 vs 26.7%; $P = .78$) hospitalizations, left ventricular (LV) end-diastolic diameter (6.4 ± 1.5 vs 6.2 ± 1.1 cm, $P = .47$), and incidence of AA (35.4% vs 33.3%; $P = .80$), VA (29% vs 26.6%; $P = .86$), and ICD shocks (22.6% vs 16.7%; $P = .93$). Beta-blocker and antiarrhythmic drug use after LVAD implantation was similar in both groups.

Conclusions: In patients with refractory HF who received CF-LVADs, CRT-D, compared with ICD, did not significantly improve mortality, all-cause hospitalization, LV dimensions, and incidence of AA and VA. (*J Cardiac Fail 2015;21:226–232*)

Key Words: Left ventricular assist device, cardiac resynchronization therapy, ICD, heart failure, ventricular arrhythmias.

Cardiac resynchronization therapy (CRT-D) and left ventricular assist devices (LVADs) provide salutary effects on ventricular remodeling. Each has been shown to improve mortality, functional status, and quality of life in patients with advanced heart failure (HF).[1–4] LVAD implantations are on the rise as a bridge to transplant, bridge to recovery, and, not infrequently, destination therapy in patients with end-stage cardiomyopathy.[5] Ventricular arrhythmias, however, are commonly seen in LVAD patients, possibly due to a combination of preexisting abnormal electrophysiologic substrate and complex electrical remodeling following LVAD implantation.[6–8] Current-generation continuous-flow LVADs (CF-LVADs) allow continued functioning of implantable cardioverter-defibrillators (ICDs) with minimal interactions.[9] Thus, the vast majority of patients with end-stage cardiomyopathy and an existing ICD continue to receive ICD therapy after LVAD implantation and in many cases undergo generator replacements during the post-LVAD period. Nonrandomized studies evaluating the survival impact of ICD therapy in LVAD recipients have had conflicting results, with 2 studies showing

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improved mortality with ICD therapy[7,10] and a 3rd showing no mortality benefit.[11]

Similarly, most patients with advanced cardiomyopathy and CRT-D who receive CF-LVADs continue to receive biventricular pacing after CF-LVAD implantation, with minimal data to support this practice. Case reports[12,13] suggest additive effects of biventricular pacing in improving outcomes in LVAD patients, but the long-term impact of continued CRT-D use on clinical outcomes in these patients remains unclear. Any benefit from CRT-D in CF-LVAD patients would be important to know, because this could affect outcomes and may aid myocardial recovery. On the other hand, lack of benefit could prompt turning off the LV lead, thus saving battery life and limiting generator replacements in this unique population.

Therefore, the objective of the present study was to evaluate whether CRT-D, compared with ICD alone, improved survival, all-cause and HF hospitalizations, and incidence of atrial (AA) and ventricular tachyarrhythmias (VA) in patients with CF-LVADs.

Materials and Methods

The present study was conducted at the University of Louisville and Jewish Hospital (Louisville, Kentucky). The study protocol was approved by the University of Louisville Institutional Review Board. Data collection and analysis were performed on 61 consecutive advanced HF patients with an existing ICD or CRT-D, who underwent CF-LVAD placement and subsequent follow-up at our institution from 2008 to 2012. Patients who underwent ICD or CRT-D implantation after LVAD implantation were excluded. All patients had CF-LVADs implanted as either bridge to transplantation or destination therapy. Patients who had LVADs implanted as bridge to recovery were excluded, because they were part of a separate clinical trial. Implanted CF-LVADs included Heartmate II (Thoratec, Pleasanton, California) in 51 patients and Heartware (Heartware International, Framingham, Massachusetts) in 10 patients.

The LVAD study population was divided into a CRT-D group where biventricular pacing was maintained after LVAD implantation (n = 31) and an ICD-only group (n = 30) composed of patients with single- and dual-chamber ICDs.

The data variables collected and analyzed included demographics, medications, etiology of HF, electrocardiographic (ECG) and echocardiographic parameters, and device-specific information on ICDs and CRT-Ds, including type of device, percentage of biventricular pacing, and incidence of ICD shocks, AA, and VA. The day of CF-LVAD implantation defined the start date for follow-up. The last day of follow-up was December 2012, date of heart transplantation, or date of death, whichever came first.

Effects of CRT-D on outcome variables were compared with CF-LVAD patients with an ICD alone. The primary outcome variables analyzed were mortality, all-cause and HF hospitalizations, and incidence of AA and VA after CF-LVAD implantation. Secondary outcome variables analyzed included incidence of ICD shocks, hospitalization for cardiac arrhythmias or ICD shocks, heart transplantation, and LVAD explantation. Patient charts were reviewed to assess use of cardiac medications during follow-up. Reported ECG and echocardiographic parameters during follow-up were assessed during the 6−12-month period after LVAD implantation. Patient medical records as well as the institutional database were reviewed to assess cause of death. Available postmortem device interrogations were reviewed to exclude an arrhythmic cause of death.

Cardiac resynchronization therapy devices were kept in the DDD(R) mode (VVIR in patients with permanent atrial fibrillation) with AV delay settings to allow consistent biventricular pacing. Adequacy of biventricular pacing before and after LVAD implantation was confirmed by means of 12-lead ECG and device interrogation. Electrocardiograms and stored device electrograms were analyzed for incidence of AA and VA. VA was defined as sustained VAs lasting >30 s or requiring ICD therapy. AA was defined as atrial tachycardia, atrial flutter, or atrial fibrillation lasting >6 hours or requiring pharmacologic or electrical therapy for termination. HF hospitalization was defined as any hospitalization secondary to clinical signs and symptoms of congestive HF (dyspnea, fatigue, volume overload, as well as use of intravenous diuretics and/or inotropes for volume) and included device malfunction (LVAD thrombosis) and aortic insufficiency−related HF.

Statistical Analysis

All numeric variables are described as mean ± SE or median with interquartile range (IQR) when appropriate. Categoric variables are presented as percentages. Continuous and categoric variables were compared between the ICD and CRT-D groups with the use of 2-sided *t* tests and chi-square tests, respectively. Kaplan-Meier curves, adjusted for baseline variables, were computed and the log-rank test used to assess survival differences between groups. A *P* value of <.05 was considered to be statistically significant. All statistical analyses were performed with the use of SAS 9.3 (SAS Institute, Cary, North Carolina).

Results

A total of 61 patients with either ICD or CRT-D underwent CF-LVAD implantation. Of these, 31 patients (age 59.8 ± 15.6 years, 83.8% male) had CRT-D and 30 patients (age 57.2 ± 13.3 years, 73.3% male) had ICD. All CRT-D patients continued to receive biventricular pacing after LVAD implantation. CF-LVAD was implanted as bridge to transplant in 27 patients and as destination therapy in 34 patients. Etiology of HF was ischemic cardiomyopathy in 37 of the 61 patients (18 [58.1%] in the CRT-D and 19 [63.3%] in the ICD group; *P* = .66). Twenty-seven patients in the CRT-D and 24 patients in the ICD group received a Heartmate II LVAD. The mean and median INTERMACS profiles for the ICD group were 2.78 and 2, respectively, and for the CRT-D group 2.66 and 2, respectively (*P* = ns).

At baseline (before LVAD implantation), no significant differences were noted between the 2 groups in demographic variables, LVAD indication, comorbid conditions, HF medications, and incidence of AA and VA (Table 1). Pre-LVAD VAs were present in 32.2% of patients in the CRT-D and 36.7% in the ICD group (*P* = .77). Thirty-seven percent of patients in the CRT-D group and 50% in the ICD group were on ≥1 class III antiarrhythmic drug