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Long-Term Results of Triventricular Versus Biventricular Pacing in Heart Failure

A Propensity-Matched Comparison

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ABSTRACT

OBJECTIVES The goal of this study was to assess the impact of triventricular pacing (Tri-V) on long-term survival.

BACKGROUND Biventricular pacing (Bi-V) is an important adjunctive treatment in advanced heart failure, but almost one-third of patients experience no improvement with this therapy and are labeled as nonresponders. Adding a third ventricular lead (Tri-V) has been shown to be feasible and provides favorable acute results when assessed by using echocardiographic, hemodynamic, and clinical endpoints. However, the long-term effects of Tri-V pacing and how it affects long-term survival remains unknown.

METHODS This single-center, propensity score–matched cohort study compared 34 patients with advanced heart failure who underwent implantation with Tri-V devices versus 34 control subjects treated with Bi-V pacing. Clinical outcomes during a median of 2,478 days (interquartile range: 1,183 to 3,214 days) were compared.

RESULTS Tri-V–treated patients compared with Bi-V–treated patients presented with a trend for shorter battery longevity (time to box change, 1,758 ± 360 days vs. 1,993 ± 408 days; $p = 0.072$). Incidence of lead dislodgement (Tri-V vs. Bi-V, 0.86 vs. 1.10 per 100 patient-years; $p = 0.742$), device-related infection (Tri-V vs. Bi-V, 1.83 vs. 1.76 per 100 patient-years; $p = 0.996$), and refractory phrenic nerve capture (Tri-V vs. Bi-V, 0.48 vs. 1.84 per 100 patient-years; $p = 0.341$) was comparable in the 2 groups. Episodes of ventricular arrhythmia requiring implantable cardioverter-defibrillator intervention occurred more frequently in the Bi-V group versus the Tri-V group (6.55 vs. 16.88 per 100 patient-years; adjusted hazard ratio: 0.31; 95% confidence interval: 0.14 to 0.66; $p = 0.002$). Lower all-cause mortality and heart transplant was observed in the Tri-V group compared with the Bi-V group (6.99 vs. 11.92 per 100 patient-years; adjusted hazard ratio: 0.44; 95% confidence interval: 0.23 to 0.85; $p = 0.015$).

CONCLUSIONS Tri-V displayed a similar safety profile compared with Bi-V and was associated with potential benefits regarding long-term survival and ventricular arrhythmia burden. (J Am Coll Cardiol EP 2016;■:■–■)

Cardiac resynchronization therapy (CRT) has emerged as one of the major developments in the treatment of advanced heart failure, providing symptom relief and improved survival benefit (1–3). Unfortunately, almost one-third of patients experience no improvement with this therapy and are labeled as nonresponders (4).

Standard CRT consists of biventricular pacing (Bi-V) from the right ventricle and coronary sinus (CS) aiming to correct electrical dyssynchrony/delayed activation of the lateral left ventricular (LV) wall (5). There are many variables that determine patient outcome to CRT, including differences in regional myocardial response to pacing, scar burden and

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

ATP = antitachycardia pacing

Bi-V = biventricular pacing

CRT = cardiac resynchronization therapy

CS = coronary sinus

ICD = implantable-cardioverter defibrillator

LV = left ventricular

RV = right ventricular

Tri-V = triventricular pacing

VF = ventricular fibrillation

VT = ventricular tachycardia

degree of myocardial recruitment, suboptimal lead positioning within scar or zones of slow conduction, and concordance with areas of latest contraction. To improve clinical outcomes and reduce the proportion of clinical nonresponders to CRT, the addition of a third ventricular lead has been used to achieve simultaneous stimulation of 3 ventricular sites and thus improve electro-mechanical synchrony (6). Compared with Bi-V pacing, this approach has been shown to improve echocardiographic and clinical responses (6,7). Whether triventricular (Tri-V) pacing affects long-term survival remains to be assessed.

METHODS

This single-center, propensity score–matched study compared the long-term clinical outcomes of patients implanted with Tri-V and Bi-V devices. Retrospective review of relevant medical records for this analysis was performed. All Tri-V–treated patients gave full informed consent, and the procedure was approved by the local ethics committee.

SETTING AND STUDY POPULATION. All consecutive patients implanted with Bi-V or Tri-V pacing devices (with or without defibrillator) at The Heart Hospital UCLH from January 2005 to December 2008 were considered potentially eligible for this analysis.

In our institution, patients underwent implantation with CRTs at the time if they had symptomatic heart failure (New York Heart Association functional class II to IV) despite maximally tolerated medical therapy, had left ventricular ejection fraction (LVEF) <35%, and had a QRS duration ≥150 ms (or QRS <150 ms with echocardiographic evidence of mechanical dyssynchrony). Patients were not considered for the purpose of this analysis if they were <18 years of age, required intravenous inotropic drug therapy, or had an estimated life expectancy <12 months due to a cause other than heart failure. Patients with unsuccessful CS lead insertion during the procedure were also excluded to preserve homogeneity while comparing groups in this as-treated analysis.

Our center's initial experience with Tri-V pacing has been published previously (7). In the initial study, during the first 12 months' post-implantation, Tri-V devices were randomly switched between 4 different pacing configurations: Tri-V; standard Bi-V; dual site LV or right ventricular (RV) pacing; and single-site RV or LV pacing. They were then programmed with the configuration providing the best echocardiographic and clinical response. Therefore, for the purpose of this as-treated analysis, Tri-V–treated patients were considered eligible if they were programmed with all 3 ventricular leads after the first 12 months (i.e., if they were receiving true Tri-V pacing). Similarly, patients in the control group had to be alive after the first year post-implantation and should be receiving effective Bi-V pacing.

Propensity score matching with a 1:1 ratio was used to obtain a control group of standard CRT patients (Bi-V group) and assure that Tri-V and their contemporary Bi-V control subjects were similar in all baseline variables. Probabilities in the Tri-V group were matched 1:1 to the best Bi-V corresponding patient.

SAMPLE CHARACTERIZATION. All variables at the time of the procedure and during follow-up were defined and categorized. Information was collected regarding demographic characteristics, anthropometric data, baseline cardiac disease, echocardiographic data, and medication.

The following variables were used for developing the propensity score, which was used for creating a well-matched control group: device type (CRT with or without a defibrillator), age at time of implant, sex, presence of atrial fibrillation (AF), pre-existing permanent pacemaker, previous valve repair or replacement, history of cancer, previous stroke, diabetes mellitus, estimated glomerular filtration rate (calculated by using the Modified Diet in Renal Disease formula), New York Heart Association functional class, primary or secondary prevention of sudden cardiac death, QRS width, bundle branch or QRS pattern, ischemic or nonischemic cardiomyopathy, LVEF, and medication (use of oral anticoagulant agents, antiplatelet agents, beta-blockers, other antiarrhythmic agents, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, spironolactone, and loop diuretic agents).

TRI-V IMPLANT PROCEDURE. Our approach to Tri-V device implantation has been described previously (7). In summary, standard, commercially available equipment (Boston Scientific, Marlborough, Massachusetts; St. Jude Medical, St. Paul, Minnesota) was used. Two different approaches were included: implanting 2 leads in the anterolateral branch of the CS and 1 in the right ventricle (group A), or implanting 1 lead in the anterolateral branch of the CS and 2 in the right ventricle (group B). All patients had a lead positioned in the RV apex, and all except for those in permanent AF had a lead positioned in the right atrium. The second RV leads in group B patients were positioned in the high RV septal location. Occlusive