The anatomic and electrical location of the left ventricular lead predicts ventricular arrhythmia in cardiac resynchronization therapy

Daniel J. Friedman, MD, Gaurav A. Upadhyay, MD, Robert K. Altman, MD, Mary Orencole, ANP-BC, Conor D. Barrett, MB, BCh, Theofanie Mela, MD, FHRS, E. Kevin Heist, MD, PhD, FHRS, Jagmeet P. Singh, MD, DPhil, FHRS

From the Cardiac Arrhythmia Service, Massachusetts General Hospital, Boston, Massachusetts.

BACKGROUND Both anatomic and electrical locations of the left ventricular (LV) lead have been identified as important predictors of clinical outcomes in cardiac resynchronization therapy (CRT). The impact of LV lead location on incident device-treated ventricular arrhythmia (VA), however, is not well understood.

OBJECTIVE To assess the relationship between electrical and anatomic LV lead location and device treated VAs in CRT.

METHODS Sixty-nine patients undergoing CRT implantation for standard indications were evaluated. Anatomic LV lead location was assessed by means of coronary venography and chest radiography and categorized as apical or nonapical. Electrical LV lead location was assessed by LV electrical delay (LVLED) and was calculated as the time between the onset of the native QRS on the surface electrocardiogram and sensed signal on the LV lead during implantation and corrected for native QRS. Incident appropriate device-treated VA was assessed via device interrogation.

RESULTS Apical lead placement was an independent predictor of VAs (hazard ratio 5.29; 95% confidence interval 1.69–16.5; $P = .004$). Among patients with a nonapical lead, LVLED $<50\%$ native QRS was an independent predictor of VAs (hazard ratio 6.90; 95% confidence interval 1.53–31.1; $P = .012$). Those with a nonapical lead and LVLED $\geq 50\%$ native QRS were at substantially lower risk for first incident and recurrent VAs when compared to all other patients.

CONCLUSIONS The apical lead position is associated with an increased risk of VAs in CRT patients. Among patients with a nonapical lead position, an LVLED of $<50\%$ of the native QRS is associated with an increased risk of VAs.

KEYWORDS Congestive heart failure; Heart failure; Cardiac resynchronization therapy; Lead; Ventricular tachycardia; Ventricular fibrillation

ABBREVIATIONS **ATP** = antitachycardia pacing; **CI** = confidence interval; **CRT** = cardiac resynchronization therapy; **CRT-D** = cardiac resynchronization therapy-defibrillator; **HR** = hazard ratio; **LBBB** = left bundle branch block; **LV** = left ventricular; **LVEDD** = left ventricular end diastolic diameter; **LVEF** = left ventricular ejection fraction; **LVESD** = left ventricular end systolic diameter; **LVLED** = left ventricular lead electrical delay; **VA** = ventricular arrhythmia; **VF** = ventricular fibrillation; **VT** = ventricular tachycardia

(Heart Rhythm 2013;10:668–675)

Introduction

Cardiac resynchronization therapy (CRT) is a well-established therapeutic modality for patients with congestive heart failure and a prolonged QRS interval on the surface electrocardiogram.[1–5] CRT has also been associated with improved electrical stability, as evidenced by a decreased risk of both atrial and ventricular arrhythmias (VAs).[6–10] Although CRT represents an important advance in the care of patients with heart failure, a substantial proportion of patients do not derive benefit from this therapy.[11] Consequently, improvements in patient selection[12] and device implantation[12,13] have become important topics of investigation.

Left ventricular (LV) lead position has emerged as an important determinant of outcomes.[12,13] Current implantation strategies typically involve anatomic targeting of the posterior or lateral wall along the short axis.[13] Additional studies have suggested that nonapical leads[14,15] and those with maximal electrical separation[16,17] may be associated with improved clinical outcomes.

Dr Heist has received honoraria from Biotronik, Boston Scientific, Sorin, and St Jude Medical; research grants from Biotronik, Sorin, and St Jude Medical; and consulting fees from Boston Scientific, Sorin, and St Jude Medical. Dr Mela has received honoraria from Boston Scientific, Medtronic, and St Jude Medical and consulting fees from St Jude Medical. Ms Orencole has received honoraria from Boston Scientific. Dr Singh has received research grants from St Jude Medical, Medtronic, Boston Scientific, and Biotronik; consulting fees from Boston Scientific, Biotronik, St Jude Medical, Medtronic, CardioInsight, Thoratec, and Biosense Webster; and honoraria from Medtronic, Biotronik, Guidant, St Jude Medical, and Sorin.
Address reprint requests and correspondence: Dr Jagmeet P. Singh, Cardiac Arrhythmia Service, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114. E-mail address: jsingh@partners.org.

1547-5271/$-see front matter http://dx.doi.org/10.1016/j.hrthm.2012.12.025

Although the relationship between optimal lead position and mortality and hospitalization has become increasingly clear, there is a paucity of data on the impact of LV lead location on incident ventricular tachycardia (VT) and ventricular fibrillation (VF) in this high-risk population. Therefore, in this study, we aimed to assess the relationship between anatomic and electrical lead location on the incidence of sustained VT and VF in patients with heart failure after CRT implantation.

Methods

Subjects

All patients implanted with cardiac resynchronization therapy-defibrillator (CRT-D) at our institution between December 2004 and September 2009 with intraprocedural left ventricular lead electrical delay (LVLED) measurements were enrolled. Patients underwent CRT-D implantation for approved indications during the enrollment period (New York Heart Association class III/IV symptoms, left ventricular ejection fraction [LVEF] $<35\%$, and QRS duration >120 ms) and were followed at our multidisciplinary CRT clinic. Patients with primary and secondary prevention ICD indications were included in the analyses.

Baseline characteristics and echocardiography

Standard echocardiographic, clinical, and demographic data were obtained for all patients. Transthoracic echocardiograms were obtained before CRT device implantation and 6 months after. LV end diastolic and end systolic dimensions (left ventricular end diastolic diameter [LVEDD] and left ventricular end systolic diameter [LVESD], respectively) were measured from the parasternal long-axis view. LV ejection fraction was calculated by using the biplane method of discs from the apical 4- and 2-chamber views.

LV lead location

Anatomic lead position was assessed via intraprocedural coronary venography and examination of posteroanterior and lateral chest x-rays obtained at the time of implantation. Lead position was classified within the long and short axes of the left ventricle. The long axis was divided into the apical, basal, and mid-ventricular segments, and the short axis was divided into the anterior, anterolateral, lateral, posterolateral, and posterior segments. For the analyses, anatomic lead location was dichotomized along the long axis into apical vs nonapical on the basis of previous work.[14,15,18]

Electrical lead position was measured intraprocedurally at the time of device implantation, as described previously.[17] Briefly, the electrical delay was calculated as the time between the onset of the QRS on the surface electrocardiogram and the sensed signal on the LV lead. This delay was indexed by the intraprocedurally measured QRS and expressed as a percentage of the baseline QRS duration. For analyses, LVLED was dichotomized by using a 50% partition on the basis of previous work.[17]

Device implantation, programming, and follow-up

CRT-D implantation, programming, and device selection was at the discretion of the treating electrophysiologist. Devices were usually programmed to initially treat VT with antitachycardia pacing (ATP), followed by high-voltage shocks if ATP was unsuccessful. VF was treated with high-voltage shocks. Detection and therapy zones were not standardized and were determined on an individual basis, although generally therapy zones began at 160–190 beats/min. Recurrent episodes of symptomatic slow VT prompted lowering of therapy zones in certain instances. All patients were followed at our institution and underwent routine device interrogations at 3–6-month intervals.

End points

The primary end point of this study was the first incident sustained VA receiving appropriate device therapy after the implantation of CRT-D. Arrhythmias were classified as VT, VF, electric storm (appropriate therapy for 3 VAs within <24 hours), or pair of arrhythmias (appropriate therapy for 2 VAs within <24 hours). All events were verified by the electrophysiologist review of device electrograms. A single episode of VA requiring multiple therapies (ie, multiple rounds of ATP, multiple rounds of shock, or ATP followed by shock(s)) for termination was classified as a single event. This end point excluded nonsustained VT and inappropriate therapies and does not imply that first therapy attempt was successful.

Statistical analysis

All analyses were performed by using SPSS software, version 20.0 (SPSS Inc, Chicago, IL). Values are presented as mean $\pm$ SD for continuous variables and as proportions for categorical variables. Differences were assessed by using Fisher exact test, Student *t* tests, or Wilcoxon rank-sum test, where appropriate. Kaplan-Meier curves were constructed to compare event rates in different subgroups and formally assessed by using log-rank testing. Univariate and multivariate analyses were performed by using Cox proportional hazards models; forward stepwise selection was used for multivariate analyses. Multivariate models adjusted for all variables in which there was a difference ($P < .10$) among the subgroups in Table 2, as well as history of VT/VF, age, LVEF $<20\%$, and sex; covariates included apical vs nonapical lead position, LVLED, age, sex, LVEDD, LVESD, hypertension (HTN), LVEF $<20\%$, and chronic atrial fibrillation. For all tests, a P value of $<.05$ was required for statistical significance.

Results

Baseline characteristics and incident device-treated arrhythmia

Sixty-nine patients (mean age 67.8 ± 12.5 years; 28% women; 52% ischemic; 9% New York Heart Association class IV symptoms; 20% with prior sustained VA) were followed for 853 ± 510 days after CRT-D implantation.