Impact of the right ventricular lead position on clinical outcome and on the incidence of ventricular tachyarrhythmias in patients with CRT-D

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BACKGROUND Data on the impact of right ventricular (RV) lead location on clinical outcome and ventricular tachyarrhythmias in cardiac resynchronization therapy with defibrillator (CRT-D) patients are limited.

OBJECTIVE To evaluate the impact of different RV lead locations on clinical outcome in CRT-D patients enrolled in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy trial.

METHODS We investigated 742 of 1089 CRT-D patients (68%) with adjudicated RV lead location enrolled in the Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy trial to evaluate the impact of RV lead location on cardiac events. The primary end point was heart failure or death; secondary end points included ventricular tachycardia (VT), ventricular fibrillation (VF), or death and VT or VF alone.

RESULTS Eighty-six patients had the RV lead positioned at the RV septal or right ventricular outflow tract region, combined as nonapical RV group, and 656 patients had apical RV lead location. There was no difference in the primary end point in patients with nonapical RV lead location versus those with apical RV lead location (hazard ratio [HR] 0.98; 95% confidence interval [CI] 0.54–1.80; $P = .983$). Echocardiographic response to CRT-D was comparable across RV lead location groups ($P > .05$ for left ventricular end-diastolic volume, left ventricular end-systolic volume, and left atrial volume percent change). However, nonapical RV lead location was associated with significantly higher risk of VT/VF/death (HR 2.45; 95% CI 1.36–4.41; $P = .003$) and VT/VF alone (HR 2.52; 95% CI 1.36–4.65; $P = .002$), predominantly in the first year after device implantation. Results were consistent in patients with left bundle branch block.

CONCLUSIONS In CRT-D patients, there is no benefit of nonapical RV lead location in clinical outcome or echocardiographic response. Moreover, nonapical RV lead location is associated with an increased risk of ventricular tachyarrhythmias, particularly in the first year after device implantation.

KEYWORDS Cardiac resynchronization therapy; Clinical outcome; Echocardiography; Ventricular arrhythmia; Nonapical RV lead position

ABBREVIATIONS **A** = atrial; **CI** = confidence interval; **CRT** = cardiac resynchronization therapy; **CRT-D** = cardiac resynchronization therapy with defibrillator; **HF** = heart failure; **HR** = hazard ratio; **ICD** = implantable cardioverter-defibrillator; **LAV** = left atrial volume; **LBBB** = left bundle branch block; **LV** = left ventricular; **LVEDV** = left ventricular end-diastolic volume; **LVEF** = left ventricular ejection fraction; **LVESV** = left ventricular end-systolic volume; **MADIT-CRT** = Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy; **RV** = right ventricular; **RVOT** = right ventricular outflow tract; **V** = ventricular; **VF** = ventricular fibrillation; **VT** = ventricular tachycardia

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Introduction

Cardiac resynchronization therapy (CRT) has been shown to improve cardiac function, clinical symptoms, and reduce heart failure (HF) hospitalization and mortality in patients with severe drug-refractory HF, and a prolonged QRS.[1–4] The Multicenter Automatic Defibrillator Implantation Trial–Cardiac Resynchronization Therapy (MADIT-CRT) trial, the Resynchronization-Defibrillation in Ambulatory

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Heart Failure Trial, and the Resynchronization Reverses Remodelling in Systolic Left Ventricular Dysfunction trial extended the indication of CRT to patients with mild HF.[5–8] Despite the growing number of CRT implantations, optimal right ventricular (RV) lead positioning remains unknown.

Small studies have indicated that placing the RV lead at the RV septum or at the right ventricular outflow tract (RVOT) might favorably affect the clinical response to CRT.[9–11] However, other studies showed no benefit of RV septal lead locations over apical RV lead positions.[12–16] This association has not yet been investigated in a larger prospective cohort of patients with mild HF.

Furthermore, we have previously shown that apical left ventricular (LV) lead location was associated with worse clinical outcome,[17] and in patients with anterior LV lead location, there was a significantly higher risk of ventricular tachyarrhythmias.[18] However, the impact of RV lead location on the risk of ventricular tachyarrhythmias has not yet been evaluated.

Therefore, the aim of our study was to assess the impact of RV lead location on HF/death, all-cause mortality, echocardiographic response, and incidence of ventricular tachyarrhythmias in cardiac resynchronization therapy with defibrillator (CRT-D) patients enrolled in the MADIT-CRT trial.

Methods

Study population

The design and protocol of the MADIT-CRT trial had been published earlier.[19] Briefly, 1820 patients with ischemic or nonischemic cardiomyopathy, left ventricular ejection fraction (LVEF) of $<30\%$, and prolonged QRS duration ≥ 130 ms were randomized to CRT-D or implantable cardioverter-defibrillator (ICD) in a 3:2 ratio. Patients were excluded from the trial as published previously.[19]

Device implantation and programming

Generally available ICD and CRT-D devices (Boston Scientific, St. Paul, MN) were implanted. RV lead positioning was left to the discretion of the investigators, with no specific recommendation in the protocol. ICD and CRT-D devices were programmed to a ventricular tachycardia (VT) zone at 180 beats/min and to a ventricular fibrillation (VF) zone at 210 beats/min. The VT zone first therapy was recommended to be programmed to antitachycardia pacing and then shock.

Patient follow-up

Patients had an outpatient visit 1 month after CRT-D or ICD implantation and every 3 months thereafter until the termination of the trial. The mean follow-up was 29.4 months. All patients had a clinical evaluation and ICD interrogation at each follow-up visit.

Evaluation of RV lead locations

The RV lead position was evaluated retrospectively from fluoroscopic multiplane images performed at the time of CRT-D device implantation, parallel with anterior/posterior and lateral chest X-ray images captured 1 day after device implantation or at the time of hospital discharge. The images were recorded on CD-ROMs and transferred to the core laboratory at the University of Rochester Medical Center for a blinded independent assessment of RV lead locations. An experienced CRT device implanting physician (H.K.) analyzed the RV lead position. The observer was unaware of the investigator-defined RV lead position. If the core laboratory observer had doubts about the accurate RV lead position, he was assisted by 2 other experienced CRT specialists (D.T.H. and S.R.) working in the same institution. The final definition of the RV lead position was achieved after all 3 observers were in agreement. The final RV lead position was assessed in the short axis view (left anterior oblique 20°–40°) along with the longitudinal axis view (right anterior oblique 20°–40°) and on the anterior/posterior and lateral chest-X ray images. The RV lead location was classified as "nonapical position" if the RV lead tip was away from the RV apex, pointing more to the posterior direction (left anterior oblique view) or to the RVOT (right anterior oblique view). The anterior/posterior and lateral chest X-ray images provided further proof of the nonapical position of the RV lead (Figure 1A). A further distinction of "RV septal" from "RVOT" lead location was considered as unreliable. RV leads positioned in the region of the RV apex were considered as "apical RV" lead location (Figure 1B). Technically adequate images permitted RV lead position assessment in 742 of 1089 patients (68%), who received CRT-D devices and were followed up for a mean of 41 ± 12 months. The following patients were not included in the current analysis: those who needed a crossover to ICD only ($n = 66$, 6.1%), those who had a crossover to CRT-D ($n = 2$, 0.2%) who never had a CRT device implanted or withdrawn before device implantation ($n = 56$, 5.1%), who underwent LV lead repositioning more than 1 week after initial CRT device implantation because of lead dislodgement ($n = 54$, 5%), those who had epicardial LV lead placement ($n = 36$, 3.3%), or cases with incomplete data sets of device implantation venograms and X-ray images ($n = 78$, 7.2%), as published previously.[17] Fifty-five patients (5%) who had changes in their device status during the long-term follow-up of the current analysis were excluded.

End points

The primary end point of the study was the first occurrence of HF/death from any cause. HF was diagnosed as signs and symptoms indicative of congestive HF, resulting in outpatient titration of oral diuretics or inpatient hospitalization for intravenous drug administration. Both HF/death and all-cause mortality were separately adjudicated by blinded independent committees, as prespecified in the study design.[19]