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Cardiac Resynchronization and Quality of Life in Patients With Minimally Symptomatic Heart Failure

Peter J. Veazie, PhD,* Katia Noyes, PhD, MPH,* Qinghua Li, MS,* W. Jackson Hall, PhD,† April Buttaccio, MPH,‡ Kelly Thevenet-Morrison, MS,* Arthur J. Moss, MD‡

Rochester, New York

Objectives This study compared the quality of life (QOL) of patients with cardiac resynchronization therapy (CRT) and an implantable cardioverter-defibrillator (ICD) to patients with an ICD only.

Background CRT with ICD is associated with a reduction in heart failure risk among minimally symptomatic patients. It is unknown whether this improves QOL.

Methods This study uses the MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) data. The MADIT-CRT enrolled 1,820 patients at 110 centers across 14 countries. Patients had ischemic cardiomyopathy (New York Heart Association [NYHA] functional class I or II) or nonischemic cardiomyopathy (NYHA functional class II only), sinus rhythm, an ejection fraction of 30% or less, and prolonged intraventricular conduction with a QRS duration of 130 ms or more. QOL was evaluated on the 1,699 patients with baseline and follow-up measures using the Kansas City Cardiomyopathy Questionnaire (KCCQ). Six dimensions (Physical Limitation, Symptom Stability, Symptom Frequency, Symptom Burden, Quality of Life, and Social Limitations) and 3 summary scores (Total Symptom, Clinical Summary, and Overall Summary) were analyzed.

Results During an average follow-up of 2.4 years, the CRT-ICD group had greater improvement than the ICD-only group on all KCCQ measures ($p < 0.05$ on each scale). These differences were significant among patients with left bundle branch block conduction disturbance ($n = 1,204$, $p < 0.01$ on each scale), but not among patients without left bundle branch block ($n = 494$).

Conclusions Compared with patients with ICD only, CRT-ICD is associated with greater improvement in QOL among relatively asymptomatic patients, specifically among those with left bundle branch conduction disturbance. (J Am Coll Cardiol 2012;60:1940–4) © 2012 by the American College of Cardiology Foundation

The MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) showed the combined cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillator (ICD), compared with ICD only, had a 34% reduction in risk of death from any cause or a nonfatal heart failure event among patients with mild heart failure (New York Heart Association [NYHA] functional classes I and II). This reduction was primarily driven by a 41% reduction in the risk of heart failure events (1). Moreover, Zareba et al. (2) and Goldenberg et al. (3) reported that CRT-ICD therapy was primarily beneficial among those with a left bundle branch block (LBBB) conduction disturbance.

In this paper, we address whether adding CRT to ICD comes at the expense of a decrease in quality of life, or whether it provides an improvement among patients with mild heart failure (NYHA functional classes I and II). We assess changes in quality of life among those with and without LBBB conduction disturbance.

Methods

Detailed information about the MADIT-CRT study design, randomization, recruitment, and outcome has been published (1,4). The MADIT-CRT trial enrolled 1,820 patients at 110 centers in 14 countries (1,271 patients in the United States) from December 22, 2004, through April 23, 2008; the trial was stopped on June 22, 2009. Patients enrolled in the study had ischemic cardiomyopathy (NYHA functional class I or II) or nonischemic cardiomyopathy (NYHA functional class II only), sinus rhythm, an ejection

From the *Department of Community and Preventive Medicine, University of Rochester Medical Center, Rochester, New York; †Department of Biostatistics and Computational Biology, University of Rochester Medical Center, Rochester, New York; and the ‡Department of Medicine, University of Rochester Medical Center, Rochester, New York. This project was funded by Boston Scientific through the MADIT-CRT project. Dr. Moss has received consulting and honorarium fees from Boston Scientific. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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fraction of 30% or less, and prolonged intraventricular conduction with a QRS duration of 130 ms or more.

The analyses presented here were based on 1,699 patients, which comprise the subset of the original 1,820 patients who had baseline observations and at least 1 additional observation on our outcome variables up to the close of the study.

Quality-of-life assessment. To assess quality of life, we used 6 basic scales and 3 summary scales of the Kansas City Cardiomyopathy Questionnaire (KCCQ) instrument that comprises heart failure–specific quality-of-life–related measures (5–11). The 6 basic scales included the Symptom Stability, Symptom Frequency, Symptom Burden, Physical Limitation, Quality of Life, and Social Limitation scales. The 3 summary scales included the Total Symptom, Clinical Summary, and Overall Summary scores. See the Online Appendix for a discussion of these scales.

Quality-of-life analysis. We used feasible generalized least squares (12) to estimate models of the KCCQ measures in which all variables are centered on hospital means, thereby eliminating hospital fixed effects, and multiplied by heteroskedasticity weights to account for the different numbers of subjects at each hospital.

The data were slightly different in baseline blood pressure across the arms; therefore, to reduce error variance, we adjusted analyses for baseline systolic and diastolic blood pressure levels.

For each KCCQ scale, we estimated 2 models: Model 1 tested the difference in the change from baseline in the CRT-ICD group compared with the change from baseline in the ICD-only group on the KCCQ scales across the 4.5 years of the study period. Model 2 tested whether the treatment effect varied across time period quintiles within the 4.5 years of the study period: joint tests were used of the interaction terms between indicators of the time quintiles and the indicator of CRT-ICD group.

LBBB subgroup analyses. We repeated the analyses of Models 1 and 2 on the LBBB and non-LBBB subgroups. We investigated whether the differences in effects were statistically different between the LBBB and non-LBBB subgroups in Model 1 by testing the interaction of the LBBB indicator and the CRT-ICD group indicator using data that included all patients.

Sensitivity analyses. See the Online Appendix for our investigation of whether date of enrollment, dying or being lost to follow-up, or the patient switching device during the study impacted the KCCQ scores differentially across study arms.

Abbreviations and Acronyms

CRT = cardiac resynchronization therapy

ICD = implantable cardioverter-defibrillator

KCCQ = Kansas City Cardiomyopathy Questionnaire

LBBB = left bundle branch block

NYHA = New York Heart Association

Results

Patient characteristics. Table 1 shows baseline characteristics and baseline KCCQ scores of the study cohort by treatment arm and LBBB status.

Quality-of-life differences and trends. Figure 1 shows the estimated difference in effects between the CRT-ICD and ICD-only groups, and the corresponding 95% confidence

Table 1 Baseline Characteristics and KCCQ Scores by Treatment Arm and LBBB Status

	All Patients*		LBBB Patients		Non-LBBB Patients	
	ICD-Only (n = 675)	CRT-ICD (n = 1,024)	ICD-Only (n = 482)	CRT-ICD (n = 722)	ICD-Only (n = 192)	CRT-ICD (n = 302)
Characteristics						
Age, yrs	64.4 ± 10.6	64.4 ± 10.8	64.4 ± 10.8	64.1 ± 10.9	64.4 ± 10.3	65.1 ± 10.7
Female, %	24%	25%	29%	32%	12%	10%
Systolic blood pressure	120.8 ± 17.7	123.8 ± 17	121.1 ± 17.6	123.9 ± 16.6	120.1 ± 18.2	123.5 ± 17.9
Diastolic blood pressure	70.7 ± 10.4	72.3 ± 10.2	70.3 ± 10.4	72.3 ± 10.0	71.5 ± 10.4	72.3 ± 10.6
NYHA functional class I†	16%	14%	12%	11%	25%	21%
Baseline KCCQ scores‡						
Symptom stability	50.3 ± 13.9	50.3 ± 14.6	50.9 ± 13.9	50.7 ± 14.0	48.7 ± 14.0	49.2 ± 16.0
Symptom frequency	81.6 ± 19.4	81.0 ± 19.7	81.8 ± 19.4	82.0 ± 18.8	81.0 ± 19.5	78.8 ± 21.6
Symptom burden	82.7 ± 18.0	82.2 ± 18.1	83.1 ± 17.7	83.0 ± 17.1	81.7 ± 18.8	80.3 ± 20.2
Physical limitation	78.1 ± 20.6	78.8 ± 19.6	78.4 ± 20.2	79.7 ± 18.6	77.3 ± 21.7	76.6 ± 21.6
Quality of life	66.4 ± 24.4	66.4 ± 23.2	66.1 ± 24.0	66.9 ± 22.5	67.4 ± 25.7	65.4 ± 24.8
Social limitation	74.1 ± 25.5	75.4 ± 23.8	74.3 ± 25.6	76.5 ± 22.7	73.6 ± 25.3	72.7 ± 26.1
Total symptom score	82.1 ± 18.0	81.6 ± 18.2	82.5 ± 17.8	82.5 ± 17.2	81.3 ± 18.4	79.5 ± 20.1
Clinical summary score	80.2 ± 17.8	80.2 ± 17.1	80.5 ± 17.5	81.1 ± 16.4	79.4 ± 18.5	78.1 ± 18.6
Overall summary score	75.2 ± 19.1	75.6 ± 18.2	75.4 ± 18.7	76.4 ± 17.4	74.9 ± 20.2	73.7 ± 19.8

Values are mean ± SD or %. Data are from patients who had baseline blood pressure measures and at least 2 KCCQ measures, including baseline. Systolic and diastolic blood pressures are the only significantly different variables between ICD-only and CRT-ICD groups for All Patients, LBBB Patients, and Non-LBBB Patients. *One individual did not have an indicated LBBB status and is included only in the All Patients results. †The percentage for NYHA functional class II classification is 100 minus the reported percent for NHYA functional class I. ‡Some scores (at most, 5%) are missing.

CRT = cardiac resynchronization therapy; ICD = implantable cardioverter-defibrillator; KCCQ = Kansas City Cardiomyopathy Questionnaire; LBBB = left bundle branch block; NYHA = New York Heart Association.