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Sex-Specific Mortality Risk by QRS Morphology and Duration in Patients Receiving CRT

Results From the NCDR

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ABSTRACT

BACKGROUND Prior studies have suggested that women have better outcomes than men after cardiac resynchronization therapy-defibrillator (CRT-D) implantation.

OBJECTIVES The purpose of this study was to compare mortality after CRT-D implantation by sex, QRS morphology, and duration.

METHODS Survival curves and covariate adjusted hazard ratios (HR) were used to assess mortality by sex in 31,892 CRT-D patients in the National Cardiovascular Data Registry (NCDR), implantable cardioverter defibrillator (ICD) registry between 2006 and 2009, with up to 5 years' follow-up (median 2.9 years, interquartile range: 2.0 to 3.9 years). Patients were grouped by QRS morphology and 10-ms increments in QRS duration.

RESULTS Among patients with left bundle branch block (LBBB), women had a 21% lower mortality risk than men (HR: 0.79; 95% CI: 0.74 to 0.84; $p < 0.001$); however, there was no sex difference in non-LBBB (HR: 0.95; 95% CI: 0.85 to 1.06; $p = 0.37$). Longer QRS duration was associated with better survival in both sexes with LBBB, but not in patients without LBBB. Compared with women with LBBB and QRS of 120 to 129 ms, women with LBBB and QRS of 140 to 149 ms had a 27% lower mortality (HR: 0.73; 95% CI: 0.60 to 0.88; $p = 0.001$); this difference was 18% in men (HR: 0.82; 95% CI: 0.71 to 0.93; $p = 0.003$). Mortality in LBBB and QRS of 150 ms or longer compared with those with LBBB and QRS of 120 to 129 ms was similar between sexes (HR: 0.61 to 0.68; $p < 0.001$ for women and HR: 0.58 to 0.66; $p < 0.001$ for men). Sex interactions within 10-ms groups were not significant.

CONCLUSIONS Among patients with LBBB who received CRT-D, mortality is lower in women than men. Additionally, longer QRS duration in LBBB is associated with better survival in both sexes. In contrast, there is no sex difference in patients without LBBB, regardless of QRS duration. Further studies should include a non-CRT comparator group to confirm these findings. (J Am Coll Cardiol 2014;64:887–94) © 2014 by the American College of Cardiology Foundation.

Biventricular pacing, a therapy for heart failure, commonly referred to as cardiac resynchronization therapy (CRT), reduces mortality and heart failure hospitalizations in selected patients with left ventricular systolic dysfunction and prolonged QRS duration (1–4). However, although there is an incomplete understanding of who benefits from CRT, all patients receiving CRT

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ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy

CRT-D = cardiac resynchronization therapy defibrillator

FDA = U.S. Food and Drug Administration

ICD = implantable cardioverter defibrillator

LBBB = left bundle branch block

NYHA = New York Heart Association

are subjected to potential device complications (e.g., infection, lead failure/dislodgement) and costs. Therefore, it is important to identify those patients most likely to benefit from this therapy.

Although most CRT clinical trials enrolled patients with a QRS duration of 120 ms or longer, meta-analyses found that benefit from CRT is most pronounced in patients with a left bundle branch block (LBBB) and QRS of 150 ms or longer (5,6). These observations are reflected in professional society guidelines, which limit Class I recommendations for CRT to patients with LBBB and QRS of 150 ms or longer. Patients with LBBB and QRS of 120 to 149 ms and those without LBBB are categorized as either Class IIa or IIb recommendations (7).

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In clinical trials of CRT, women only represent approximately 20% of patients; therefore, the results of both the trials and meta-analyses primarily reflect outcomes in men. Nonetheless, previous studies suggest that benefit from CRT is greater in women (8–11). This may be due to a combination of reasons, including that women are more likely to have LBBB and nonischemic cardiomyopathy, which are both associated with a better CRT response (12). Furthermore, separate analyses suggest that one-third of patients with LBBB by conventional electrocardiographic (ECG) criteria may not have true LBBB (13–16). Because women have a shorter QRS duration than men in the absence of any conduction disease (17), they can have a true LBBB at a shorter QRS duration than men (16). Previous studies suggest that sex-specific QRS duration criteria for LBBB predict a better response to CRT (18,19).

This study assessed the effect of CRT by sex in a large real-world CRT-defibrillator (CRT-D) population. The objective was to compare long-term mortality outcomes of women and men receiving CRT-D among different combinations of QRS morphology and duration.

METHODS

This study included all patients in the National Cardiovascular Data Registry (NCDR), implantable cardioverter defibrillator (ICD) registry who received a CRT-D device between January 1, 2006, and September 30, 2009 (n = 178,900). The registry, formed in 2005 with data collection beginning in 2006, contains data on all ICD and CRT-D implantations from more than 80% of hospitals in the United States (20). Patient-level clinical, demographic, and procedural information was collected using standardized data elements and definitions. The NCDR programs use a multistage data quality process, including quality checks on submitted data, outlier analysis, and medical record audits (21). The ICD Registry is used in more than 1,400 US hospitals, including almost all centers that implant cardiac rhythm devices (22).

The defined endpoint for this study was time to death from any cause obtained by linking NCDR registry files with the Social Security Death Master File. Patients were censored if they were alive at the end of the follow-up period (March 31, 2011). We excluded patients with a QRS of <120 ms or >220 ms, epicardial leads, a history of atrial fibrillation, or a prior pacemaker or ICD; those who received a CRT-D device for secondary prevention of sudden cardiac death or had missing data on sex, QRS morphology, or duration; patients who could not be linked to the Death Master File; and those who were not admitted to the hospital for the sole purpose of CRT-D implantation. Prior pacemaker or ICD (n = 66,122) and hospital admission for reasons other than CRT-D implantation (n = 50,753) accounted for most of the 147,008 exclusions (82% of all identified registry patients). Patients with QRS of greater than 220 ms were excluded due to the small number of subjects in this category and uncertainty about the accuracy of QRS duration measurement. Patients who were not admitted for the sole purpose of CRT-D implantation were excluded based on a potential confounding effect of competing factors for death. Finally, the study population was restricted to patients without atrial fibrillation, as atrial fibrillation is associated with a low rate of biventricular pacing. The U.S.

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