JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 66, NO. 23, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.09.097

Comparative Effectiveness of CRT-D Versus Defibrillator Alone in HF Patients With Moderate-to-Severe Chronic Kidney Disease

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ABSTRACT

BACKGROUND Patients with moderate-to-severe chronic kidney disease (CKD) are poorly represented in clinical trials of cardiac resynchronization therapy (CRT).

OBJECTIVES This study sought to assess the real-world comparative effectiveness of CRT with defibrillator (CRT-D) versus implantable cardioverter-defibrillator (ICD) alone in CRT-eligible patients with moderate-to-severe CKD.

METHODS We conducted an inverse probability-weighted analysis of 10,946 CRT-eligible patients (ejection fraction <35%, QRS >120 ms, New York Heart Association functional class III/IV) with stage 3 to 5 CKD in the National Cardiovascular Data Registry (NCDR) ICD Registry, comparing outcomes between patients who received CRT-D (n = 9,525) versus ICD only (n = 1,421). Outcomes were obtained via Medicare claims and censored at 3 years. The primary endpoint of heart failure (HF) hospitalization or death and the secondary endpoint of death were assessed with Cox proportional hazards models. HF hospitalization, device explant, and progression to end-stage renal disease were assessed using Fine-Gray models.

RESULTS After risk adjustment, CRT-D use was associated with a reduction in HF hospitalization or death (hazard ratio [HR]: 0.84; 95% confidence interval [CI]: 0.78 to 0.91; $p < 0.0001$), death (HR: 0.85; 95% CI: 0.77 to 0.93; $p < 0.0004$), and HF hospitalization alone (subdistribution HR: 0.84; 95% CI: 0.76 to 0.93; $p < 0.009$). Subgroup analyses suggested that CRT was associated with a reduced risk of HF hospitalization and death across CKD classes. The incidence of in-hospital, short-term, and mid-term device-related complications did not vary across CKD stages.

CONCLUSIONS In a nationally representative population of HF and CRT-eligible patients, use of CRT-D was associated with a significantly lower risk of the composite endpoint of HF hospitalization or death among patients with moderate-to-severe CKD in the setting of acceptable complication rates. (J Am Coll Cardiol 2015;66:2618–29)

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Manuscript received June 30, 2015; revised manuscript received September 17, 2015, accepted September 21, 2015.

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Advanced symptomatic heart failure (HF) and chronic kidney disease (CKD) are frequently comorbid and represent 2 of the most challenging and costly diseases for individuals, families, and societies. Approximately 60% of Medicare patients with HF have stage 3 or greater CKD (1). Annual HF expenditures in the United States are approximately $30 billion, and this is expected to rise to $53 billion by 2030 (2). Although improvements in HF care via pharmacological neurohormonal modulation have improved longevity and quality of life for the overall population of HF patients, these therapies are often contraindicated, poorly tolerated, or of reduced efficacy among patients with advanced CKD.

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Over the past decade, cardiac resynchronization therapy (CRT) has emerged as an important therapy for patients with a prolonged QRS and moderate-to-severe medication-refractory systolic HF. Multiple large randomized trials have demonstrated that CRT can reduce HF symptoms, HF hospitalizations, and death (3–6). These landmark studies either excluded or did not report outcomes among patients with advanced (stages 3b to 5) CKD (7). Data on CRT in advanced CKD are currently limited to small, retrospective, single-center studies (8,9) and a single meta-analysis (10). Concerns regarding the potential for decreased CRT efficacy and increased complications may lower the rate of CRT use in patients with advanced CKD. Thus, optimal device strategy for this population remains unclear (11) and variability in practice exists (12).

To address this important gap in knowledge, we performed an observational comparative effectiveness analysis comparing outcomes among CRT-eligible patients who received a CRT with implantable cardioverter-defibrillator (ICD) versus ICD alone in the National Cardiovascular Data Registry (NCDR) ICD Registry. We hypothesized that CRT would be associated with a lower risk in HF hospitalizations and death, but the magnitude of effect may be attenuated based on severity of CKD.

METHODS

DATA SOURCES. NCDR ICD Registry. Patients for this study were selected from the NCDR ICD Registry, a national registry that included approximately 90% of all ICD implantations in the United States (13). All Medicare beneficiaries receiving a primary prevention ICD are enrolled in the ICD registry according to a mandate from the Centers for Medicare & Medicaid Services. The ICD registry includes extensive information on baseline patient characteristics and in-hospital outcomes. Rigorous data abstraction processes and standards have been published and include electronic data submission via a secure website, standardized variable definitions, electronic quality checks, and annual on-site audits of 10% of enrolling sites (14). This approach has led to >90% accuracy for data elements (15).

Medicare database. Longitudinal outcomes were obtained by linking fee-for-service Medicare claims to the ICD registry using a previously validated methodology (16) with indirect identifiers: hospital, patient sex, birth date, admission date, and discharge date. Inpatient claims, outpatient claims, and the denominator files were used to assess morbidity and mortality. We used the Chronic Conditions Warehouse database (years 2005 to 2011), which includes both Part A and Part B Medicare claims to assess specific covariates and outcomes.

STUDY POPULATION. We restricted the study population to all fee-for-service Medicare patients ≥65 years old with stage 3 to 5 CKD (glomerular filtration rate [GFR] <60 ml/min/1.73 m^2, including those on dialysis) who underwent ICD implantation (with or without CRT) between January 1, 2006, and December 31, 2009; were eligible for CRT based on contemporary indications during the study period (ejection fraction [EF] <35%, QRS >120 ms, New York Heart Association [NYHA] functional class III/IV); and could be linked to Medicare claims data. We excluded patients who were admitted during a non-elective hospitalization, were enrolled in the ICD registry at the time of generator change, required an epicardial lead, or had a prior pacemaker or defibrillator.

PATIENT CHARACTERISTICS. All baseline characteristics except for the frailty and dementia variables were directly obtained from the ICD registry case report form. Dementia was defined by the presence of a diagnosis from either of 2 Hierarchical Condition Categories (HCCs): "dementia" or "senility, nonpsychotic organic brain syndromes/conditions." Frailty/disability was defined by the following HCCs: protein-calorie malnutrition; quadriplegia, other extensive paralysis; paraplegia; spinal cord disorders/injuries; hemiplegia/hemiparesis; legally blind; decubitus ulcer of skin; chronic ulcer of skin, except decubitus; vertebral fractures; amputation status, lower limb amputation; and amputation status, upper limb. Missing variables were addressed with the multiple imputation technique; the coefficients of

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CKD = chronic kidney disease

CRT = cardiac resynchronization therapy

CRT-D = cardiac resynchronization therapy with defibrillator

EF = ejection fraction

ESRD = end-stage renal disease

GFR = glomerular filtration rate

HCC = Hierarchical Condition Categories

HF = heart failure

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

ICD-9 = International Classification of Diseases-Ninth Revision-Clinical Modification

LBBB = left bundle branch block

NYHA = New York Heart Association