Annals of Internal Medicine | ORIGINAL RESEARCH

Comparative Effectiveness of Cardiac Resynchronization Therapy With an Implantable Cardioverter-Defibrillator Versus Defibrillator Therapy Alone

A Cohort Study

Frederick A. Masoudi, MD, MSPH; Xiaojuan Mi, PhD; Lesley H. Curtis, PhD; Pamela N. Peterson, MD, MSPH; Jeptha P. Curtis, MD; Gregg C. Fonarow, MD; Stephen C. Hammill, MD; Paul A. Heidenreich, MD; Sana M. Al-Khatib, MD, MHS; Jonathan P. Piccini, MD, MHS; Laura G. Qualls, MS; and Adrian F. Hernandez, MD, MHS

Background: Trials comparing implantable cardioverter-defibrillator (ICD) therapy with cardiac resynchronization therapy with a defibrillator (CRT-D) are limited to selected patients treated at centers with extensive experience.

Objective: To compare outcomes after CRT-D versus ICD therapy in contemporary practice.

Design: Retrospective cohort study using the National Cardiovascular Data Registry's ICD Registry linked with Medicare claims.

Setting: 780 U.S. hospitals implanting both CRT-D and ICD devices.

Patients: 7090 propensity-matched patients older than 65 years with reduced left ventricular ejection fraction (<0.35) and prolonged QRS duration on electrocardiography (≥120 ms) having CRT-D or ICD implantation between 1 April 2006 and 31 December 2009.

Measurements: Risks for death, readmission, and device-related complications over 3 years.

Results: Compared with ICD therapy, CRT-D was associated with lower risks for mortality (cumulative incidence, 25.7% vs. 29.8%; adjusted hazard ratio [HR], 0.82 [99% CI, 0.73 to 0.93]), all-cause readmission (cumulative incidence, 68.6% vs. 72.8%; adjusted HR, 0.86 [CI, 0.81 to 0.93]), cardiovascular readmission (cumulative incidence, 45.0% vs. 52.4%; adjusted HR, 0.80 [CI, 0.73 to 0.88]), and heart failure readmission (cumulative incidence, 24.3% vs. 29.4%; adjusted HR, 0.78 [CI, 0.69 to 0.88]). It was also associated with greater risks for device-related infection (cumulative incidence, 1.9% vs. 1.0%; adjusted HR, 1.90 [CI, 1.07 to 3.37]). The lower risks for heart failure readmission associated with CRT-D compared with ICD therapy were most pronounced among patients with left bundle branch block or a QRS duration at least 150 ms and in women.

Limitations: Patients were not randomly assigned to treatment groups, and few patients could be propensity-matched. The findings may not extend to younger patients or those outside of fee-for-service Medicare.

Conclusion: In older patients with reduced left ventricular ejection fraction and prolonged QRS duration, CRT-D was associated with lower risks for death and readmission than ICD therapy alone.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2014;160:603-611. www.annals.org

For author affiliations, see end of text.

Implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) have changed the management of patients with reduced left ventricular ejection faction (LVEF). Guidelines for device-based treatment recommend ICD therapy for many patients with reduced LVEF (1) on the basis of randomized, controlled trials showing mortality benefits of ICD therapy (2–7). Cardiac resynchronization therapy with an ICD (CRT-D), which involves the placement of an additional coronary sinus lead capable of pacing the left ventricle, is further recommended for selected patients with an LVEF of 0.35 or less, heart failure, and evidence of ventricular dyssynchrony manifested as QRS prolongation on electrocardiography (1). The recommendations are based on evidence of lower risk for worsening heart failure and, in some cases, lower mortality with CRT-D in these selected groups (1).

Although randomized clinical trials have identified important incremental benefits of CRT in selected patients, the comparative effectiveness of CRT-D versus ICD therapy has not been characterized in patients cared for in clinical practice. Clinical trials in patients with cardiovascular disease in general (8, 9) and of device therapy in particular (10, 11) have typically enrolled selected patients who differ from those seen in practice. Device trials are also often performed in sites and by clinicians with substantial expertise, which may reduce complication rates (12). This factor is specifically germane to CRT because implanting the additional left ventricular lead is associated with higher rates of complications than ICD therapy alone (13).

Differences in the patients selected for therapy and the centers where the procedures are done could influence the outcomes of device therapy in real-world clinical practice. Given the number of ICD and CRT devices implanted in the United States annually (14), understanding the incremental effectiveness and complications of CRT in patients treated in contemporary practice could have important implications for patients, clinicians, and policymakers.

Controversies about the optimum use of CRT persist. Although the benefits are clearest and recommendations for its use are strongest in patients with left bundle branch block (LBBB) and a QRS duration greater than 150 ms, the benefits in patients with other intraventricular conduc-

Context

In randomized, controlled trials, cardiac resynchronization therapy with a defibrillator (CRT-D) decreased mortality in patients with reduced left ventricular ejection fraction and prolonged QRS duration compared with implantable cardioverter-defibrillator (ICD) therapy alone. The relative benefits and harms of these devices in more routine practice settings have not been studied.

Contribution

The investigators compared CRT-D with ICD in more than 7000 patients enrolled in a patient registry and found that CRT-D decreased mortality more than ICD. Device-related infections were more common with CRT-D.

Caution

Residual confounding could not be eliminated.

Implication

Real-world performance of CRT-D versus ICD seems similar to that observed in randomized, controlled trials.

—The Editors

tion delays (for example, right bundle branch block) and less prolonged QRS duration are debated (1). Furthermore, the benefits of CRT have generally been greatest in patients with more severe symptoms of heart failure, but recent trials have suggested meaningful benefits in less symptomatic patients (6, 7, 15). Finally, questions about the effectiveness of CRT according to patient sex (6, 16) or in patients with atrial fibrillation (1) have been raised.

We performed an observational comparative effectiveness study of CRT-D versus ICD therapy alone in a contemporary cohort of patients with reduced LVEF and electrocardiographic evidence of ventricular dyssynchrony who were receiving device-based therapy. Our objectives were to characterize the associations between CRT-D versus ICD therapy alone and patient outcomes, including death, hospitalizations, and device-related complications, and to investigate these associations in specific subgroups of clinical interest.

METHODS

Data Sources

Data were from the National Cardiovascular Data Registry's ICD Registry and the Centers for Medicare & Medicaid Services' Medicare claims data. The ICD Registry was established in 2005 through a partnership of the Heart Rhythm Society and the American College of Cardiology Foundation and became the sole repository of ICD implantation data for Medicare beneficiaries on 1 April 2006. The Centers for Medicare & Medicaid Services mandates that hospitals enter data on all Medicare beneficiaries receiving ICD therapy for primary prevention into the registry (14), which contains patient demographic characteristics, detailed medical history, and clinical and procedural information.

The registry uses standardized data definitions and data quality monitoring (17). Medicare data include inpatient and outpatient claims and the corresponding denominator files between 2006 and 2011. We linked the registry data to Medicare claims data using a validated method that involves combinations of indirect identifiers (18). The Institutional Review Board of the Duke University Health System (Durham, North Carolina) approved the study.

Study Cohort

In the linked data set, we identified patients who were 65 years or older; were admitted specifically for first-time device implantation; were discharged home between 1 April 2006 and 31 December 2009; were enrolled in fee-for-service Medicare at discharge; and might be considered for CRT-D on the basis of a history of heart failure, an LVEF of 0.35 or less, and a QRS duration at least 120 ms. We excluded patients who received device therapy for secondary prevention, received epicardial leads, were admitted for reasons other than device implantation, had coronary revascularization during the index admission, had a prior ICD pacemaker, or had myocardial infarction within 40 days before the index discharge.

Treatment

The treatments of interest were CRT-D and ICD therapy alone as recorded in the registry. The registry does not include data for patients receiving CRT without a defibrillator; thus, this therapy was not considered.

Outcomes

The outcomes of interest were the occurrence of and time to all-cause mortality; all-cause readmission; and readmission for cardiovascular disease, heart failure, device-related infection, and mechanical complications requiring system revision for up to 3 years after implantation. We ascertained mortality on the basis of death dates in the Medicare denominator files and readmission on the basis of subsequent Medicare inpatient claims (**Appendix Table 1**, available at www.annals.org).

Subgroups

We prespecified clinically important subgroups—including age, sex, race, and type of intraventricular conduction delay—combined with QRS duration, New York Heart Association class, and the presence or absence of atrial fibrillation and renal dysfunction. We also considered subgroups according to the cause of left ventricular systolic dysfunction (ischemic vs. nonischemic). We combined the type of intraventricular conduction delay and QRS duration and classified patients into 1 of 4 categories according to guidelines for device-based therapy: LBBB and QRS duration 150 ms or greater, LBBB and QRS duration 120 to 149 ms, no LBBB and QRS duration 150 ms or greater, and no LBBB and QRS duration 120 to 149 ms (1). For the purposes of subgroup analysis, we categorized renal

function into 4 groups on the basis of estimated glomerular filtration rates of 90 mL/min/1.73 m^2 or greater, 60 to 89 mL/min/1.73 m^2, 30 to 59 mL/min/1.73 m^2, and 29 mL/min/1.73 m^2 or less or end-stage renal disease (19).

Covariates

We obtained covariates of interest from the registry, including demographic characteristics, medical history, results of clinical measures, year of implantation, and discharge medications. We considered patients to be receiving optimal medical therapy if they received a β-blocker and an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker in the absence of contraindications. Demographic variables were complete, and the other variables were missing at low rates (<1%). To avoid case-wise deletions, we imputed missing continuous variables to the overall median value and missing categorical variables to the most common response, an approach that is considered appropriate for variables with low rates of missing data (20).

Statistical Analysis

We described the baseline characteristics of the study population by using frequencies with percentages for categorical variables and means with SDs for continuous variables. We tested for differences between treatment groups using the chi-square test for categorical variables and the *t* test for continuous variables. We calculated the standardized difference expressed in percentage points between 2 treatment groups as the difference in means or proportions divided by a pooled estimate of the SD. Standardized differences less than 10 percentage points suggest balance in the 2 groups with respect to that variable (21).

We estimated the cumulative incidence of each outcome at 1 year and 3 years after device implantation for both treatment groups. Estimates of mortality were based on the Kaplan–Meier estimator, and differences between groups were assessed using log-rank tests. Estimates of readmission were based on the cumulative incidence function, which accounts for the competing risk for mortality. For patients not having an event, we defined a censoring date as the earliest among the end of follow-up at 1 year or 3 years after the index discharge date, the end of claims data availability on 31 December 2011, or the date on which the patient enrolled in a Medicare managed care plan. We used Gray tests to assess differences between treatment groups (22).

We used propensity score matching to account for differences in observed covariates between treatment groups (23). We estimated propensity scores by fitting a nonparsimonious logistic regression model with receipt of CRT-D as the dependent variable, the baseline preprocedural characteristics described earlier as independent variables, and site-level annual volume of device procedures as a covariate. Medical therapies at discharge were considered as covariates in the multivariable models but not for determining propensity.

We matched patients who received ICD therapy to those who received CRT-D in a 1:1 ratio using a greedy matching algorithm with a maximum allowable difference of 0.05 and matched within site of implantation. Patients who could not be matched using these criteria were removed from the analysis; as a sensitivity analysis, we conducted propensity matching without a restriction for site of implantation (that is, "across-hospital" matching). We used Cox proportional hazards models to estimate the associations between the matched treatment groups and each outcome. Significance tests and CIs were based on robust SEs to account for the clustering of patients by hospital.

To estimate treatment effects within subgroups, we included interaction terms between the subgroup variable and the treatment indicator in the models and tested the significance of the interaction terms. We estimated the association between treatment and each outcome within each subgroup by using model contrasts. Because of the large number of comparisons, we used a 2-tailed α level of 0.01 and corresponding 99% CIs for all comparisons.

We used SAS, version 9.2 (SAS Institute, Cary, North Carolina), for all analyses. We used procedure PROC PHREG to estimate the relationship between device type and outcomes. For propensity score matching, we used an SAS macro (gmatch.sas) provided by Mayo clinical staff (www.mayo.edu/research/departments-divisions/department-health-sciences-research/division-biomedical-statistics-informatics/software/locally-written-sas-macros).

Role of the Funding Source

This study was funded by the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services, American College of Cardiology Foundation's National Cardiovascular Data Registry, American College of Cardiology Foundation, and Heart Rhythm Society. The funding source had no role in the design, conduct, or reporting of this study. The study was reviewed and approved by the Research and Publications Committee of the National Cardiovascular Data Registry ICD Registry.

RESULTS

The eligible study cohort included 29 777 patients in 1450 hospitals meeting study enrollment criteria having first-time device implantation between 2006 and 2009, of whom 21 319 received CRT-D and 8458 received ICD therapy alone. More than one third (37.4%) of the hospitals were teaching hospitals, the median annual volume of procedures was 61 (interquartile range, 22 to 131), and the median number of certified beds was 304 (interquartile range, 196 to 446). **Appendix Table 2** (available at www.annals.org) shows the number of patients and hospitals in the overall cohort, the across-hospital propensity-matched cohort, and the within-hospital propensity-matched cohort. Standardized differences between recipients of

CRT-D and recipients of ICD therapy in the unmatched cohorts exceeded 10 percentage points for many characteristics (**Appendix Table 3**, available at www.annals.org).

The propensity score models included 25 variables and resulted in a matched cohort of 3545 patients in each group in 780 hospitals; **Appendix Figure 1** (available at www.annals.org) shows propensity distributions for the 2 groups. In the propensity-matched cohort, the standardized differences in characteristics between the CRT-D and ICD groups did not exceed 5.8 percentage points for any measured variable and were lower than those in the unmatched cohort for many variables, supporting the assumption that measured characteristics were balanced between the groups (**Table 1**; **Appendix Table 4**, available at www.annals.org).

In the propensity-matched cohort, the cumulative incidence rates and hazards of mortality and all-cause readmission were lower in the CRT-D group (**Table 2** and **Figure**). Specifically, at 3 years, the CRT-D group had a lower cumulative incidence of death (25.7% vs. 29.8%; difference, −4.1 percentage points; adjusted hazard ratio [HR], 0.82 [99% CI, 0.73 to 0.93]; $P < 0.001$) and all-cause readmission (68.6% vs. 72.8%; difference, −4.2 percentage points; adjusted HR, 0.86 [CI, 0.81 to 0.93]; $P < 0.001$). It was also associated with a lower cumulative incidence of cardiovascular readmission (45.0% vs. 52.4%; difference, −7.4 percentage points; adjusted HR, 0.80 [CI, 0.73 to 0.88]; $P < 0.001$) and heart failure readmission (24.3% vs. 29.4%; difference, −5.1 percentage points; adjusted HR, 0.78 [CI, 0.69 to 0.88]; $P < 0.001$) (**Figure**).

Patients receiving CRT-D had higher rates of device-related infection than ICD recipients (1.9% vs. 1.0%; difference, 0.9 percentage point; adjusted HR, 1.90 [CI, 1.07 to 3.37]; $P = 0.004$) (**Figure**), and the risks for mechanical device complications did not significantly differ (2.3% vs. 1.7%; difference, 0.6 percentage point; adjusted HR, 1.39 [CI, 0.89 to 2.19]; $P = 0.058$) (**Figure**). Cumulative incidences and survival curves for these outcomes in the unmatched cohort and the across-hospital propensity-matched cohort are shown in **Appendix Table 5** and **Appendix Figures 2** and **3** (available at www.annals.org).

Subgroup analysis in the propensity-matched cohort showed no significant interactions between device type and the prespecified subgroups with respect to mortality or all-cause readmission (that is, the relationship between device type and these outcomes did not differ significantly according to subgroup strata) (**Appendix Figures 4** to **7**, available at www.annals.org). For cardiovascular readmission, the risk among CRT-D recipients was lower than that for ICD recipients in the strata with LBBB regardless of QRS duration ($P = 0.004$ for the interaction) (**Appendix Figures 4** to **7**). For heart failure readmission, the risk among CRT-D recipients was lower than that for ICD recipients in the strata with LBBB regardless of QRS duration ($P = 0.006$ for the interaction) and in women ($P = 0.002$) (**Appendix Figure 4**). With respect to device-related adverse outcomes, we observed no significant interactions between device type and the prespecified subgroups ($P > 0.010$ for all interactions; data not shown).

Discussion

In this observational study of patients who were eligible for CRT-D according to established criteria, those who received CRT-D had significantly lower risks for death and readmission than those who received ICD therapy alone. Associations between CRT-D and lower hazards of cardiovascular and heart failure readmission were greater among patients with a longer QRS duration or LBBB. The association between CRT-D and lower hazards of heart failure readmission was greater among patients with a longer QRS duration or LBBB and among women. Cardiac resynchronization therapy with a defibrillator was associated with significantly greater hazards of device-related infection compared with ICD therapy alone.

Our findings are relevant to current practice guidelines for device-based therapy (1). The better readmission outcomes with CRT-D that we observed in patients with LBBB and QRS duration greater than 150 ms are consistent with existing guidelines (American College of Cardiology Foundation/American Heart Association/Heart Rhythm Society [ACCF/AHA/HRS] class I recommendation, level of evidence: A). However, the guideline recommendations are more qualified for patients with LBBB and QRS duration 120 to 150 ms (ACCF/AHA/HRS class IIa recommendation, level of evidence: B, for patients with New York Heart Association class II to IV symptoms) and patients with no LBBB and QRS duration greater than 150 ms (ACCF/AHA/HRS class IIa recommendation, level of evidence: A, for patients with New York Heart Association class III or IV symptoms), for whom we found a positive association between CRT-D and outcomes. Our finding of little benefit among patients without LBBB and a QRS duration between 120 and 150 ms is consistent with the current ACCF/AHA/HRS class III recommendation that CRT-D is not useful in this population. Randomized trials to clarify the incremental benefits, if any, of CRT-D over ICD therapy alone in patients without LBBB and with a relatively narrow QRS complex would further inform treatment decisions in these subgroups.

Results within subgroups of patients are also relevant because of questions about the benefits of CRT as a function of baseline QRS duration and morphologic characteristics. Subgroup analyses in MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) and RAFT (Resynchronization-Defibrillation for Ambulatory Heart Failure Trial) suggested greater benefits of CRT among patients with LBBB and QRS duration 150 ms or greater (6, 7). Meta-analyses of the trials further supported these findings

Table 1. **Baseline Characteristics of the Within-Hospital Propensity-Matched Cohort**

Characteristic	ICD (*n* = 3545)	CRT-D (*n* = 3545)	*P* Value	Standardized Difference, *percentage points*
Mean age (SD), *y*	74.9 (6.0)	74.6 (6.0)	0.041	4.9
Age group, *n (%)*			0.31	2.4
65–79 y	2697 (76.1)	2733 (77.1)		
≥80 y	848 (23.9)	812 (22.9)		
Men, *n (%)*	2555 (72.1)	2552 (72.0)	0.94	0.2
Race, *n (%)*			0.74	1.8
Black	273 (7.7)	258 (7.3)		
White	3153 (88.9)	3173 (89.5)		
Other/unknown	119 (3.4)	114 (3.2)		
Medical history, *n (%)*				
Atrial fibrillation or flutter	1164 (32.8)	1101 (31.1)	0.109	3.8
Diabetes mellitus	1309 (36.9)	1352 (38.1)	0.29	2.5
Cerebrovascular disease	571 (16.1)	562 (15.9)	0.77	0.7
Chronic lung disease	798 (22.5)	790 (22.3)	0.82	0.5
Heart failure duration			0.44	3.0
≤3 mo	437 (12.3)	420 (11.8)		
3–9 mo	545 (15.4)	582 (16.4)		
>9 mo	2563 (72.3)	2543 (71.7)		
Hypertension	2762 (77.9)	2771 (78.2)	0.80	0.6
Ischemic heart disease	2513 (70.9)	2419 (68.2)	0.015	5.8
Nonischemic dilated cardiomyopathy	1099 (31.0)	1173 (33.1)	0.060	4.5
Prior CABG	1551 (43.8)	1497 (42.2)	0.195	3.1
Prior heart failure hospitalization	1697 (47.9)	1683 (47.5)	0.74	0.8
Prior myocardial infarction			0.96	0.1
No	1657 (46.7)	1655 (46.7)		
>40 d	1888 (53.3)	1890 (53.3)		
Prior PCI	1132 (31.9)	1083 (30.6)	0.21	3.0
Renal failure, dialysis	107 (3.0)	108 (3.0)	0.94	0.2
Syncope	332 (9.4)	300 (8.5)	0.182	3.2
Clinical measures				
NYHA functional class, *n (%)*			0.162	5.3
I	103 (2.9)	97 (2.7)		
II	1041 (29.4)	1056 (29.8)		
III	2321 (65.5)	2283 (64.4)		
IV	80 (2.3)	109 (3.1)		
Intraventricular conduction, *n (%)*			0.87	2.6
LBBB	1864 (52.6)	1906 (53.8)		
RBBB	617 (17.4)	594 (16.8)		
Delay, nonspecific	503 (14.2)	485 (13.7)		
Normal	401 (11.3)	401 (11.3)		
Other	160 (4.5)	159 (4.5)		
Mean ejection fraction (SD)	0.25 (0.06)	0.25 (0.06)	1.00	0.0
Mean QRS duration (SD), *ms*	149 (23.1)	149 (19.6)	0.71	0.9
Mean systolic blood pressure (SD), *mm Hg*	134 (22.4)	134 (22.3)	0.65	1.1
Laboratory test results				
Mean blood urea nitrogen level (SD)				
mmol/L	9.3 (5.0)	9.2 (4.7)	–	–
mg/dL	26.1 (13.9)	25.8 (13.1)	0.27	2.6
Mean creatinine level (SD)				
μmol/L	123.8 (70.7)	123.8 (97.3)	–	–
mg/dL	1.4 (0.8)	1.4 (1.1)	0.49	1.6
Mean sodium level (SD), *meq/L*	139 (3.3)	139 (3.3)	0.82	0.6
Mean eGFR (SD), *mL/min/1.73/m²**	59.6 (23.8)	59.5 (22.0)	0.87	0.4
Year of procedure, *n (%)*			0.70	2.8
2006	806 (22.7)	767 (21.6)		
2007	1054 (29.7)	1083 (30.6)		
2008	858 (24.2)	869 (24.5)		
2009	827 (23.3)	826 (23.3)		

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Table 1—Continued

Characteristic	ICD (*n* = 3545)	CRT-D (*n* = 3545)	*P* Value	Standardized Difference, *percentage points*
Discharge medications, *n (%)*				
ACE inhibitor or ARB	2787 (78.6)	2764 (78.0)	0.51	1.6
β-Blocker	3028 (85.4)	3030 (85.5)	0.95	0.2
Digoxin	887 (25.0)	923 (26.0)	0.33	2.3
Diuretic	2500 (70.5)	2563 (72.3)	0.098	3.9
Optimal medical therapy†	2446 (69.0)	2411 (68.0)	0.37	2.1
Mean hospital annual device volume (SD), *n (%)*	232 (6.5)	232 (6.5)	0.91	1.7

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CABG = coronary artery bypass graft; CRT-D = cardiac resynchronization therapy with a defibrillator; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RBBB = right bundle branch block.
* The eGFR was calculated as follows: 186 × (serum creatinine level at admission) − 1.154 × (age) − 0.203 × (0.742 for women) × (1.210 for black patients).
† β-Blocker and ACE inhibitor/ARB in the absence of contraindications.

(24, 25). Observational studies, including one from the National Cardiovascular Data Registry, have generally been limited to patients who received CRT and suggest that patients with LBBB and longer QRS duration have the best survival rates. However, these studies did not include a comparator group receiving ICD therapy to provide insights into the relative outcomes of CRT-D and ICD therapy in subgroups according to QRS duration and morphologic characteristics (26–29).

Our understanding of the benefits of CRT as a function of patient symptom status at implantation has evolved over time. Many trials of CRT were restricted to patients with severe symptoms of heart failure (4). More recently, RAFT and MADIT-CRT identified benefits of CRT in patients with less severe symptoms (6, 7); a meta-analysis of existing trials of CRT further supports these findings (15). In our observational study, CRT was associated with similarly lower risks for mortality and heart failure readmission across the spectrum of symptoms.

Our study also informs debates about the benefits of CRT-D according to patient sex and the presence of atrial fibrillation. Post hoc analyses of clinical trial data suggest that women may be more likely than men to benefit from CRT-D (6, 16). Consistent with these findings, we identified a significantly greater difference in the rates of heart failure readmission associated with CRT-D versus ICD therapy among women than among men. In addition, current guideline recommendations for CRT among patients with chronic atrial fibrillation reserve this therapy for those expected to require frequent ventricular pacing (1). We did not find a significantly greater difference in the lower risk for cardiovascular readmission with CRT-D among patients without atrial fibrillation. However, interpretation of this finding is limited, because the ICD Registry does not distinguish between permanent and paroxysmal atrial fibrillation.

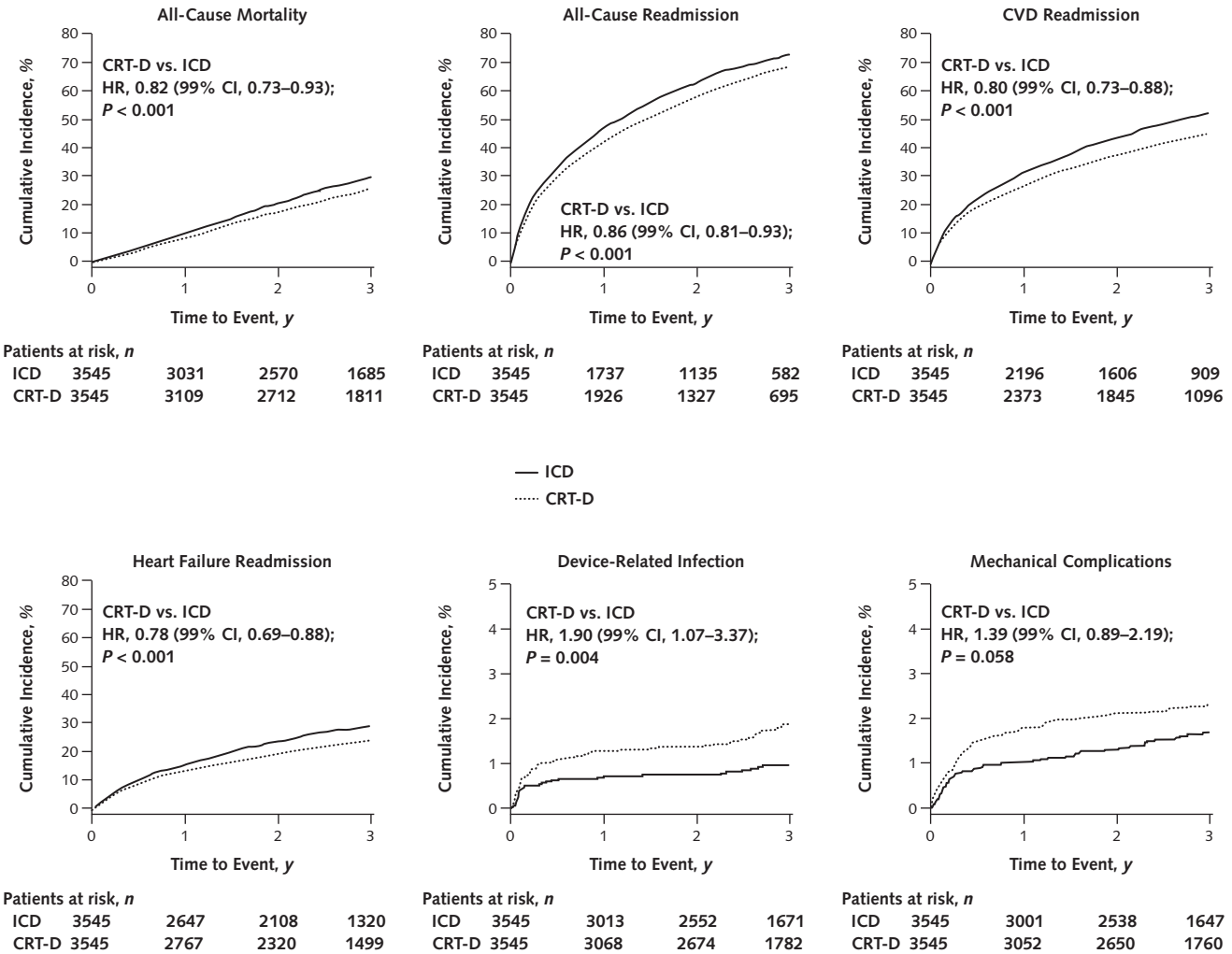
Although CRT may provide important benefits, this therapy may also result in higher rates of device-related complications, because CRT devices require an additional lead to pace the left ventricle placed in the coronary sinus. In RAFT, complications defined as adverse events deemed attributable to device implantation were higher with CRT-D than with ICD therapy alone at 30 days (13.8% vs. 6.4%) (7). In MADIT-CRT, rates of complications at 30 days were higher among patients who received CRT-D than those who received ICD therapy alone. These complications included pneumothorax (1.7% vs. 0.8%), infection (1.1% vs. 0.7%), pocket hematoma requiring evacuation (3.3% vs. 2.5%), and complications related to the coronary sinus lead (4.5% vs. 0%) (6). The rates of infectious complications associated with CRT-D in our study were significantly higher than those associated with ICD

Table 2. **Cumulative Incidence of Study Outcomes in the Within-Hospital Propensity-Matched Cohort***

Event	1 y After Device Implantation			3 y After Device Implantation		
	ICD	CRT-D	*P* Value†	ICD	CRT-D	*P* Value†
Death	346 (10.0)	287 (8.3)	0.012	954 (29.8)	828 (25.7)	<0.001
All-cause readmission	1649 (47.4)	1479 (42.3)	<0.001	2445 (72.8)	2307 (68.6)	<0.001
Cardiovascular readmission	1084 (31.1)	937 (26.8)	<0.001	1745 (52.4)	1509 (45.0)	<0.001
Heart failure readmission	547 (15.8)	472 (13.5)	0.010	972 (29.4)	810 (24.3)	<0.001
Device-related infection	24 (0.7)	45 (1.3)	0.012	32 (1.0)	62 (1.9)	0.002
Mechanical complications	36 (1.0)	63 (1.8)	0.007	56 (1.7)	79 (2.3)	0.049

CRT-D = cardiac resynchronization therapy with a defibrillator; ICD = implantable cardioverter-defibrillator.
* *n* = 7090. Values reported are number of events (cumulative incidence per 100 patients at risk).
† *P* values are from log-rank tests for death and from Gray tests for all other outcomes.

Figure. **Cumulative incidence in the within-hospital propensity-matched cohort.**



The cohort included 7090 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; CVD = cardiovascular disease; HR = hazard ratio; ICD = implantable cardioverter-defibrillator.

therapy; as in RAFT and MADIT-CRT, CRT-D was associated with lower overall rates of death and hospitalization than ICD therapy regardless of the risks for complications (6, 7).

Our study provides a unique perspective on associations between CRT and outcomes above and beyond ICD therapy in contemporary practice. Patients who receive device therapy in the community differ from those enrolled in clinical trials (10). Furthermore, clinical trials of invasive procedures are often done at centers with greater procedural experience than those where patients in community practice receive therapy (12). Because it is reasonable to believe that the effectiveness and safety of invasive therapies vary as a result of patients' age and comorbid conditions and operator experience, studies that assess the comparative effectiveness of these therapies in real-world populations are critical complements to clinical trials.

Certain limitations should be considered in the interpretation of our findings. First, patients were not randomly assigned to treatment, so the observed associations may reflect the influence of residual confounding. Although we used robust analytic approaches, we could not account for unmeasured differences. Second, the propensity-matched analysis included only a few members of the original cohort. Third, the cohort consisted of fee-for-service Medicare beneficiaries aged 65 years or older, potentially limiting the extent to which the findings apply to younger populations or enrollees in Medicare managed care plans. However, because older populations with associated comorbid conditions have been underrepresented in clinical trials, this study provides a perspective on a clinically important population. Finally, we could not assess outcomes in patients receiving CRT without a defibrillator or evaluate functional outcomes or quality of life. However, we

observed strong associations between mortality and readmission consistent with the findings of clinical trials in selected populations.

In this observational study of patients with reduced LVEF and prolonged QRS duration, CRT-D was associated with lower rates of death and readmission than ICD therapy alone despite higher rates of device-related infections. The associations between CRT-D and hospitalizations for heart failure were most pronounced in patients with LBBB or QRS duration 150 ms or greater or both and in women. These findings complement those of randomized trials that established the benefits of CRT-D in selected populations.

From the University of Colorado Anschutz Medical Campus, Aurora, Colorado; Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina; Denver Health Medical Center, Denver, Colorado; Yale University School of Medicine, New Haven, Connecticut; Ahmanson–University of California, Los Angeles, Cardiomyopathy Center, Los Angeles, California; Mayo Clinic, Rochester, Minnesota; and Veterans Affairs Palo Alto Healthcare System, Palo Alto, California.

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Acknowledgment: The authors thank Damon M. Seils, MA, from Duke University, who provided editorial assistance and prepared the manuscript.

Financial Support: By contract HHSA290200500321 (Duke University Developing Evidence to Inform Decisions about Effectiveness Center) from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services, as part of the Developing Evidence to Inform Decisions about Effectiveness program, and the American College of Cardiology Foundation's National Cardiovascular Data Registry. The ICD Registry is an initiative of the American College of Cardiology Foundation and the Heart Rhythm Society. Dr. Peterson is supported by grant K08HS019814 from the Agency for Healthcare Research and Quality.

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M13-1879.

Reproducible Research Statement: *Study protocol and statistical code:* Available from Dr. Curtis (e-mail, lesley.curtis@duke.edu). *Data set:* Available at www.ncdr.com/research.

Requests for Single Reprints: Frederick A. Masoudi, MD, MSPH, Division of Cardiology, University of Colorado Anschutz Medical Campus, Box B132, Room 522, 12401 East 17th Avenue, Aurora, CO 80045; e-mail, fred.masoudi@ucdenver.edu.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Dr. Masoudi: Division of Cardiology, Anschutz Medical Campus, Box B132, Room 522, 12401 East 17th Avenue, Aurora, CO 80045.
Drs. Mi, Curtis, Al-Khatib, Piccini, Qualls, and Hernandez: Duke Clinical Research Institute, PO Box 17969, Durham, NC 27715.
Dr. Peterson: Division of Cardiology, Denver Health Medical Center, Box 0960, 777 Bannock Street, Denver, CO 80204.
Dr. Curtis: Yale School of Medicine, PO Box 208056, 333 Cedar Street, New Haven, CT 06520-8056.
Dr. Fonarow: Ahmanson–University of California, Los Angeles, Cardiomyopathy Center, 200 UCLA Medical Plaza, Suite 224, Los Angeles, CA 90095.
Dr. Hammill: Division of Cardiovascular Diseases, Mayo Clinic, 200 First Street SW, Rochester, MN 55905.
Dr. Heidenreich: Veterans Affairs Palo Alto Medical Center, 111C Cardiology, 3801 Miranda Avenue, Palo Alto, CA 94304.

Author Contributions: Conception and design: F.A. Masoudi, L.H. Curtis, G.C. Fonarow, S.M. Al-Khatib, L.G. Qualls, A.F. Hernandez.
Analysis and interpretation of the data: F.A. Masoudi, X. Mi, L.H. Curtis, J.P. Curtis, G.C. Fonarow, P.A. Heidenreich, S.M. Al-Khatib, J.P. Piccini, A.F. Hernandez.
Drafting of the article: F.A. Masoudi, X. Mi.
Critical revision of the article for important intellectual content: F.A. Masoudi, L.H. Curtis, P.N. Peterson, J.P. Curtis, G.C. Fonarow, S.C. Hammill, P.A. Heidenreich, S.M. Al-Khatib, J.P. Piccini, L.G. Qualls, A.F. Hernandez.
Final approval of the article: F.A. Masoudi, L.H. Curtis, P.N. Peterson, J.P. Curtis, G.C. Fonarow, S.C. Hammill, P.A. Heidenreich, S.M. Al-Khatib, J.P. Piccini, A.F. Hernandez.
Provision of study materials or patients: G.C. Fonarow.
Obtaining of funding: L.H. Curtis, A.F. Hernandez.
Administrative, technical, or logistic support: L.H. Curtis, S.C. Hammill, L.G. Qualls, A.F. Hernandez.
Collection and assembly of data: F.A. Masoudi, G.C. Fonarow, S.C. Hammill.

Appendix Table 1. **Definitions of Readmission Outcomes**

Outcome	Diagnosis and Procedure Codes
Readmission for any cause	Inpatient admissions excluding transfers to or from another hospital and admissions for rehabilitation (ICD-9-CM diagnosis code V57.xx or DRG 462 before 1 October 2007 or DRG 945 or 946 after 1 October 2007)
Cardiovascular readmission	DRGs 104–112, 115–118, 121–145, 479, 514–518, 525–527, 535, 536, and 547–558 before 1 October 2007 and DRGs 215–238, 242–254, 258–262, and 280–316 on or after 1 October 2007
Heart failure readmission	DRG 127 before 1 October 2007 and DRGs 291–293 on or after 1 October 2007 on an inpatient claim
Readmission for device-related infection	ICD-9-CM diagnosis code 996.61 in any position on an inpatient claim
Readmission for mechanical device complications requiring system revision	ICD-9-CM diagnosis code 996.04 or 996.01 combined with procedure code 37.75, 37.79, 37.97, 37.99, or 00.52 on an inpatient claim

DRG = diagnosis-related group; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

Appendix Table 2. **Counts of Patients and Hospitals in the Unmatched, Across-Hospital Propensity-Matched, and Within-Hospital Propensity-Matched Cohorts**

Variable	Unmatched	Across-Hospital Propensity-Matched	Within-Hospital Propensity-Matched
Patients	29 777	10 962	7090
Hospitals	1231	1121	780
Hospitals doing both CRT-D and ICD	982	797	780

CRT-D = cardiac resynchronization therapy with a defibrillator; ICD = implantable cardioverter-defibrillator.

Appendix Table 3. Baseline Characteristics of the Unmatched Cohort

Characteristic	ICD (*n* = 8457)	CRT-D (*n* = 21 316)	*P* Value	Standardized Difference, *percentage points*
Mean age (SD), *y*	74.5 (6.0)	74.8 (6.0)	<0.001	5.3
Age group, *n (%)*			<0.001	5.2
65–79 y	6588 (77.9)	16 139 (75.7)		
≥80 y	1870 (22.1)	5180 (24.3)		
Men, *n (%)*	6401 (75.7)	14 413 (67.6)	<0.001	18.0
Race, *n (%)*			0.91	0.6
Black	568 (6.7)	1447 (6.8)		
White	7611 (90.0)	19 151 (89.8)		
Other/unknown	279 (3.3)	721 (3.4)		
Medical history, *n (%)*				
Atrial fibrillation or flutter	2595 (30.7)	6708 (31.5)	0.190	1.7
Diabetes mellitus	2981 (35.2)	8041 (37.7)	<0.001	5.1
Hypertension	6591 (77.9)	16 624 (78.0)	0.92	0.1
Cerebrovascular disease	1322 (15.6)	3113 (14.6)	0.029	2.9
Chronic lung disease	1733 (20.5)	4989 (23.4)	<0.001	7.0
Heart failure duration			0.188	2.3
≤3 mo	983 (11.6)	2360 (11.1)		
3–9 mo	1388 (16.4)	3400 (15.9)		
>9 mo	6087 (72.0)	15 559 (73.0)		
Ischemic heart disease	6166 (72.9)	13 616 (63.9)	<0.001	19.5
Nonischemic dilated cardiomyopathy	2429 (28.7)	8123 (38.1)	<0.001	20.0
Prior heart failure hospitalization	3703 (43.8)	11 177 (52.4)	<0.001	17.4
Prior myocardial infarction			<0.001	19.2
No	3596 (42.5)	11 095 (52.0)		
>40 d	4862 (57.5)	10 224 (48.0)		
Renal failure, dialysis	238 (2.8)	579 (2.7)	0.64	0.6
Syncope	808 (9.6)	1797 (8.4)	0.002	3.9
Clinical measures				
NYHA functional class, *n (%)*			<0.001	128.4
I	537 (6.3)	183 (0.9)		
II	4898 (57.9)	2340 (11.0)		
III	2910 (34.4)	18 014 (84.5)		
IV	113 (1.3)	782 (3.7)		
Intraventricular conduction, *n (%)*			<0.001	61.5
LBBB	3397 (40.2)	14 432 (67.7)		
RBBB	1622 (19.2)	2670 (12.5)		
Delay, nonspecific	1439 (17.0)	2116 (9.9)		
Normal	1652 (19.5)	1308 (6.1)		
Other	348 (4.1)	793 (3.7)		
Mean ejection fraction (SD)	0.26 (0.06)	0.24 (0.06)	<0.001	22.0
Mean QRS duration (SD), *ms*	145 (21.7)	153 (20.8)	<0.001	37.3
Mean systolic blood pressure (SD), *mm Hg*	135 (22.2)	133 (22.3)	<0.001	7.9
Laboratory test results				
Mean blood urea nitrogen level (SD)				
mmol/L	8.9 (4.5)	9.4 (4.9)	–	–
mg/dL	24.9 (12.6)	26.4 (13.7)	<0.001	10.9
Mean creatinine level (SD)				
μmol/L	123.8 (70.7)	123.8 (79.6)	–	–
mg/dL	1.4 (0.8)	1.4 (0.9)	0.023	3.0
Mean sodium level (SD), *meq/L*	139 (3.2)	139 (3.4)	<0.001	5.7
Year of procedure, *n (%)*				3.1
2006	1967 (23.3)	4365 (20.5)		
2007	2518 (29.8)	5908 (27.7)		
2008	2083 (24.6)	5399 (25.3)		
2009	1890 (22.3)	5647 (26.5)		

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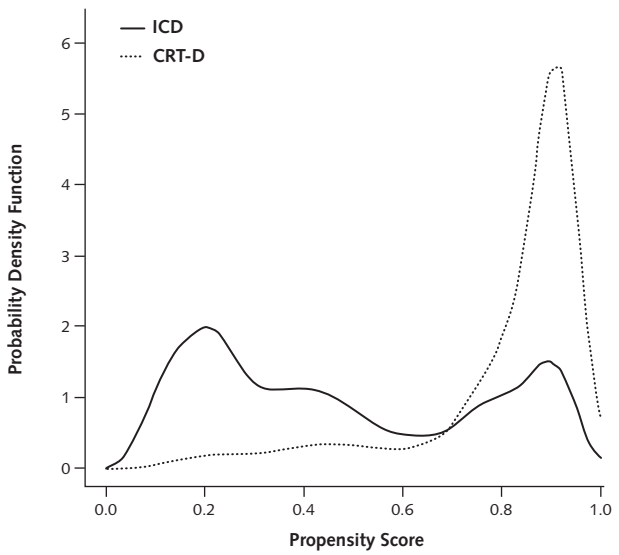
Appendix Table 3—**Continued**

Characteristic	ICD (*n* = 8457)	CRT-D (*n* = 21 316)	*P* Value	Standardized Difference, *percentage points*
Discharge medications, *n* (%)				
ACE inhibitor or ARB	6736 (79.6)	16 716 (78.4)	0.017	3.0
β-Blocker	7292 (86.2)	18 483 (86.7)	0.27	1.4
Diuretic	2035 (24.1)	5909 (27.7)	<0.001	8.4
Digoxin	5657 (66.9)	15 872 (74.5)	<0.001	16.7
Optimal medical therapy*	5934 (70.2)	14 722 (69.1)	0.058	2.4

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CRT-D = cardiac resynchronization therapy with a defibrillator; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association; RBBB = right bundle branch block.
* β-Blocker and ACE inhibitor/ARB in the absence of contraindications.

Appendix Figure 1. **Distribution of propensity scores in the unmatched cohort.**



The cohort included 29 777 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; ICD = implantable cardioverter-defibrillator.

Appendix Table 4. **Baseline Characteristics of the Across-Hospital Propensity-Matched Cohort**

Characteristic	ICD (*n* = 5472)	CRT-D (*n* = 5472)	*P* Value	Standardized Difference, *percentage points*
Mean age (SD), *y*	74.9 (6.0)	74.7 (6.0)	0.040	3.9
Age group, *n (%)*			0.24	2.2
65–79 y	4159 (76.0)	4211 (77.0)		
≥80 y	1313 (24.0)	1261 (23.0)		
Men, *n (%)*	3940 (72.0)	3893 (71.1)	0.32	1.9
Race, *n (%)*			0.98	0.4
Black	381 (7.0)	377 (6.9)		
White	4899 (89.5)	4900 (89.5)		
Other/unknown	192 (3.5)	195 (3.6)		
Medical history, *n (%)*				
Atrial fibrillation or flutter	1739 (31.8)	1725 (31.5)	0.77	0.6
Diabetes mellitus	1959 (35.8)	1982 (36.2)	0.65	0.9
Cerebrovascular disease	853 (15.6)	841 (15.4)	0.75	0.6
Chronic lung disease	1169 (21.4)	1194 (21.8)	0.56	1.1
Heart failure duration			0.28	3.1
≤3 mo	651 (11.9)	685 (12.5)		
3–9 mo	890 (16.3)	932 (17.0)		
>9 mo	3931 (71.8)	3855 (70.4)		
Hypertension	4245 (77.6)	4259 (77.8)	0.75	0.6
Ischemic heart disease	3768 (68.9)	3713 (67.9)	0.26	2.2
Nonischemic dilated cardiomyopathy	1791 (32.7)	1857 (33.9)	0.19	2.6
Prior heart failure hospitalization	2567 (46.9)	2567 (46.9)	1.00	0.0
Prior myocardial infarction			0.17	2.6
No	2590 (47.3)	2661 (48.6)		
>40 d	2882 (52.7)	2811 (51.4)		
Renal failure, dialysis	156 (2.9)	174 (3.2)	0.31	1.9
Syncope	525 (9.6)	499 (9.1)	0.39	1.6
Clinical measures				
NYHA functional class, *n (%)*			0.70	2.3
I	189 (3.5)	183 (3.3)		
II	2260 (41.3)	2287 (41.8)		
III	2910 (53.2)	2874 (52.5)		
IV	113 (2.1)	128 (2.3)		
Intraventricular conduction, *n (%)*			0.86	2.2
LBBB	2917 (53.3)	2966 (54.2)		
RBBB	869 (15.9)	838 (15.3)		
Delay, nonspecific	718 (13.1)	722 (13.2)		
Normal	737 (13.5)	726 (13.3)		
Other	231 (4.2)	220 (4.0)		
Mean ejection fraction (SD)	0.25 (0.06)	0.25 (0.06)	0.28	2.1
Mean QRS duration (SD), *ms*	148 (22.7)	149 (20.1)	0.31	1.9
Mean systolic blood pressure (SD), *mm Hg*	134 (22.2)	134 (22.0)	0.74	0.6
Laboratory test results				
Mean blood urea nitrogen level (SD)				
mmol/L	9.1 (4.7)	9.1 (4.7)	–	–
mg/dL	25.6 (13.2)	25.6 (13.2)	0.80	0.5
Mean creatinine level (SD)				
μmol/L	123.8 (70.7)	123.8 (79.6)	–	–
mg/dL	1.4 (0.8)	1.4 (0.9)	0.81	0.5
Mean sodium level (SD), *meq/L*	139 (3.3)	139 (3.3)	0.98	0.0
Year of procedure, *n (%)*			0.46	3.1
2006	1269 (23.2)	1211 (22.1)		
2007	1608 (29.4)	1609 (29.4)		
2008	1319 (24.1)	1319 (24.1)		
2009	1276 (23.3)	1333 (24.4)		

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Appendix Table 4—Continued

Characteristic	ICD (n = 5472)	CRT-D (n = 5472)	P Value	Standardized Difference, *percentage points*
Discharge medications, *n (%)*				
ACE inhibitor or ARB	4338 (79.3)	4323 (79.0)	0.72	0.7
β-Blocker	4707 (86.0)	4714 (86.1)	0.85	0.4
Digoxin	1371 (25.1)	1449 (26.5)	0.088	3.3
Diuretic	3802 (69.5)	3829 (70.0)	0.57	1.1
Optimum medical therapy*	3817 (69.8)	3799 (69.4)	0.71	0.7

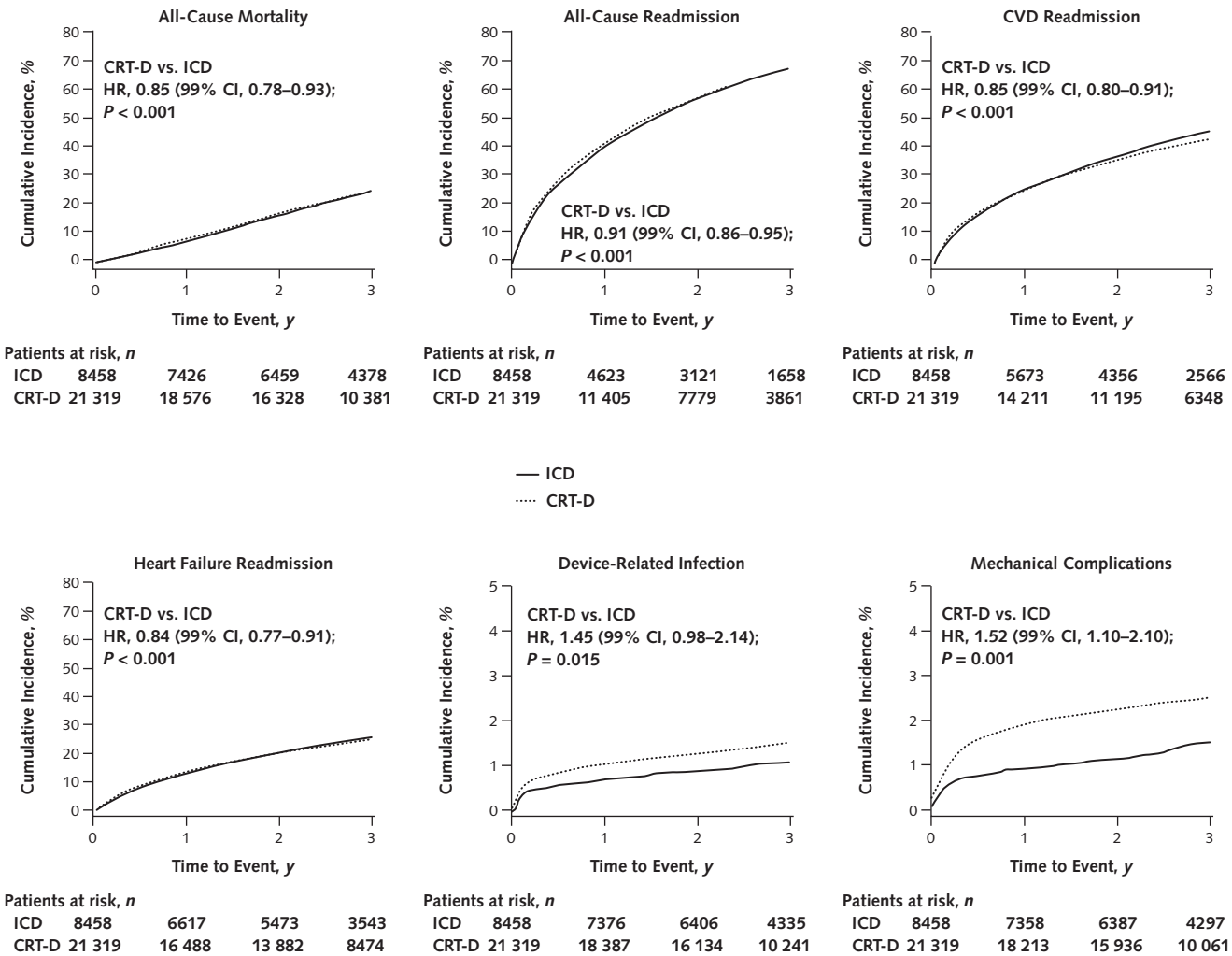
ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CRT-D = cardiac resynchronization therapy with a defibrillator; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association; RBBB = right bundle branch block.
* β-Blocker and ACE inhibitor/ARB in the absence of contraindications.

Appendix Table 5. Cumulative Incidence of Study Outcomes in the Unmatched and Across-Hospital Propensity-Matched Cohorts*

Event	1 y After Device Implantation			3 y After Device Implantation		
	ICD	CRT-D	P Value†	ICD	CRT-D	P Value†
Unmatched cohort (n = 29 773)						
Death	637 (7.7)	1810 (8.7)	0.007	1934 (25.3)	4898 (25.4)	0.56
All-cause readmission	3460 (41.7)	8993 (42.9)	0.015	5503 (68.9)	13 926 (69.2)	0.173
Cardiovascular readmission	2187 (26.3)	5560 (26.5)	0.53	3724 (46.9)	8874 (44.2)	0.004
Heart failure readmission	1082 (13.1)	2877 (13.8)	0.098	2027 (25.7)	4961 (24.9)	0.36
Device-related infection	59 (0.7)	224 (1.1)	0.005	89 (1.1)	313 (1.6)	0.005
Mechanical complications	76 (0.9)	404 (1.9)	<0.001	118 (1.5)	510 (2.5)	<0.001
Across-hospital propensity-matched cohort (n = 10 944)						
Death	485 (9.1)	405 (7.6)	0.006	1205 (27.6)	1030 (24.0)	<0.001
All-cause readmission	2393 (44.5)	2191 (40.7)	<0.001	3438 (70.5)	3232 (67.2)	<0.001
Cardiovascular readmission	1541 (28.6)	1375 (25.6)	<0.001	2353 (49.0)	2099 (44.1)	<0.001
Heart failure readmission	786 (14.6)	698 (13.0)	0.016	1314 (27.8)	1129 (24.1)	<0.001
Device-related infection	39 (0.7)	67 (1.2)	0.006	55 (1.1)	86 (1.7)	0.008
Mechanical complications	58 (1.1)	79 (1.5)	0.072	84 (1.8)	117 (2.5)	0.018

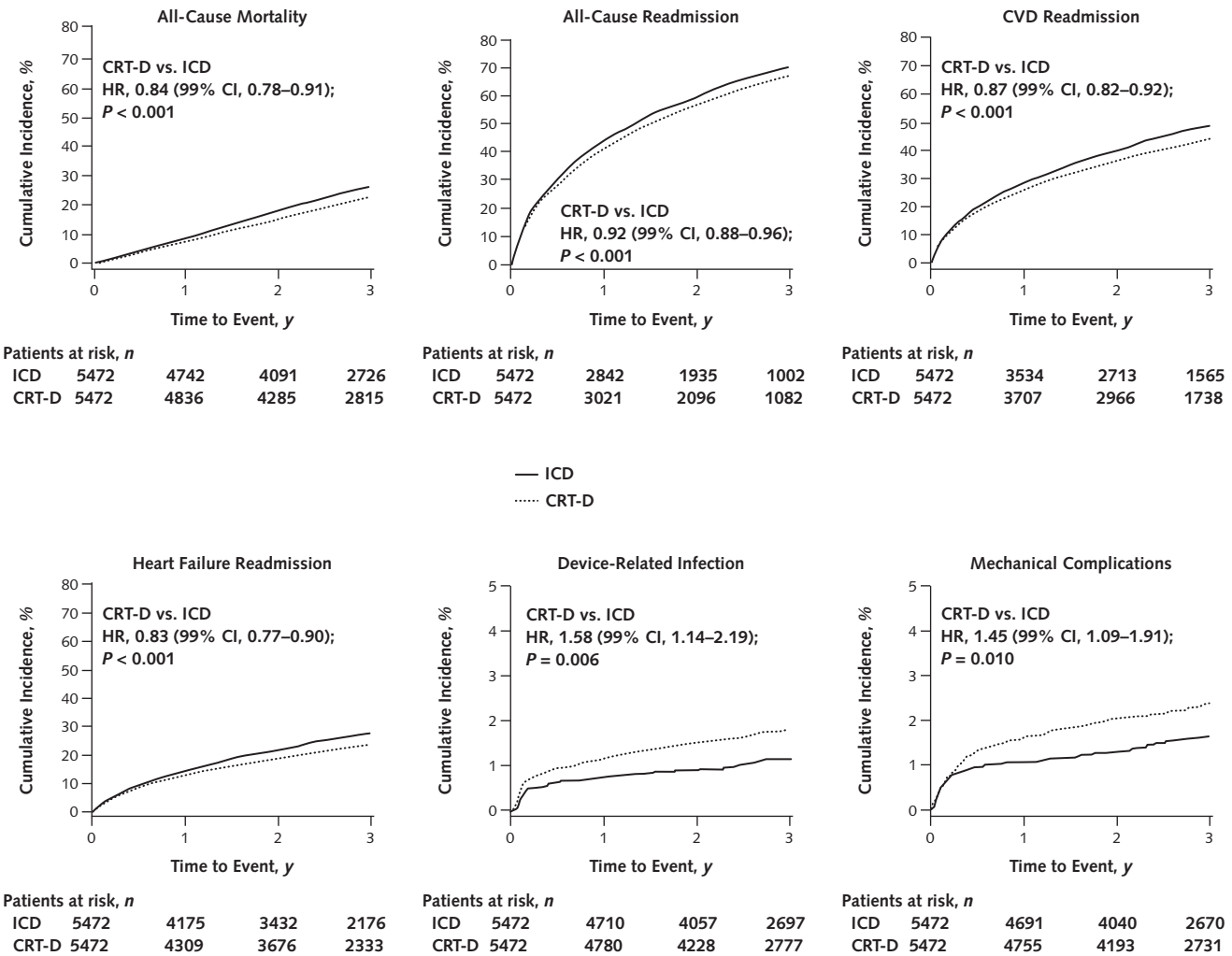
* Values reported are number of events (cumulative incidence per 100 patients at risk).
† P values are from log-rank tests for death and from Gray tests for all other outcomes.

Appendix Figure 2. **Cumulative incidence in the unmatched cohort.**



The cohort included 29 777 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; CVD = cardiovascular disease; HR = hazard ratio; ICD = implantable cardioverter-defibrillator.

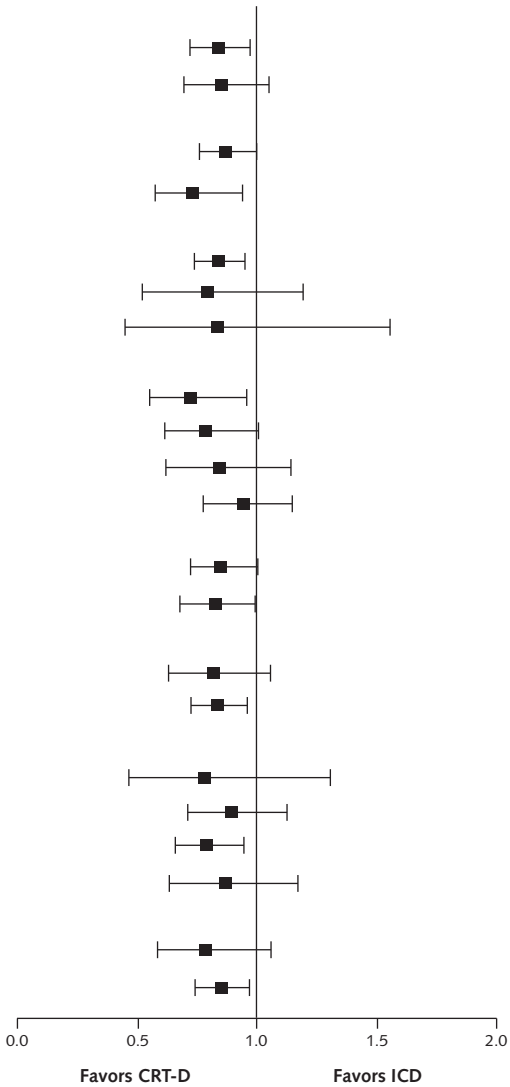
Appendix Figure 3. **Cumulative incidence in the across-hospital propensity-matched cohort.**



The cohort included 10 944 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; CVD = cardiovascular disease; HR = hazard ratio; ICD = implantable cardioverter-defibrillator.

Appendix Figure 4. **Associations between CRT-D versus ICD therapy alone and mortality in the within-hospital propensity-matched cohort, by patient characteristic.**

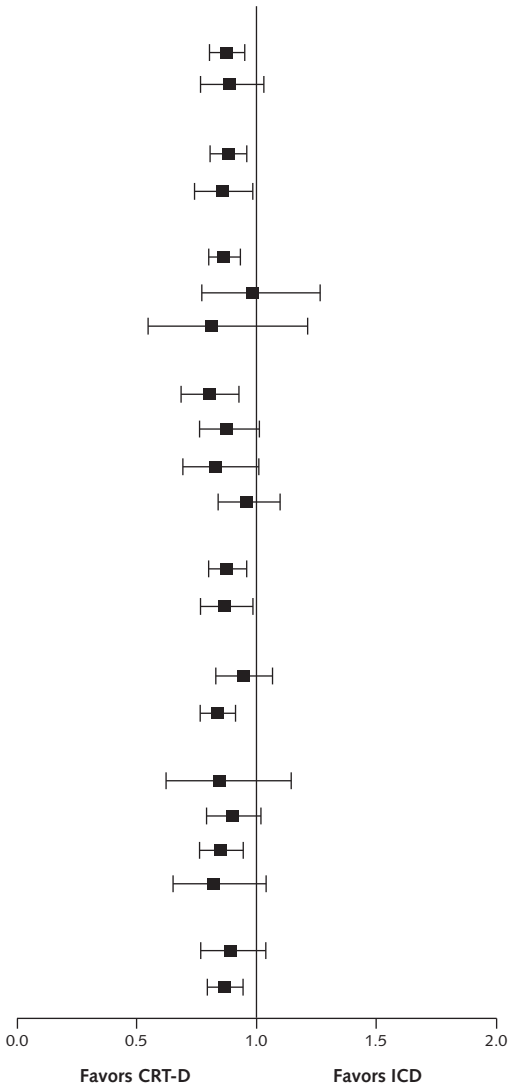
Subgroup	Patients, *n* (%)	CRT-D vs. ICD Hazard Ratio (99% CI)	*P* Value
Age			
65–79 y	5430 (77)	0.82 (0.71–0.96)	0.86
≥80 y	1660 (23)	0.84 (0.68–1.04)	
Sex			0.117
Men	5107 (72)	0.86 (0.74–0.99)	
Women	1983 (28)	0.72 (0.56–0.92)	
Race			0.94
White	6326 (89)	0.83 (0.73–0.94)	
Black	531 (7)	0.78 (0.51–1.19)	
Other/unknown	233 (3)	0.83 (0.44–1.54)	
LBBB/QRS duration			0.22
LBBB/QRS >150 ms	1913 (27)	0.72 (0.55–0.94)	
LBBB/QRS of 120–149 ms	1857 (26)	0.78 (0.61–1.00)	
No LBBB/QRS >150 ms	1120 (16)	0.84 (0.62–1.13)	
No LBBB/QRS of 120–149 ms	2200 (31)	0.94 (0.77–1.14)	
Atrial fibrillation			0.74
No	4825 (68)	0.84 (0.72–0.99)	
Yes	2265 (32)	0.81 (0.67–0.99)	
NYHA functional class			0.83
I–II	2297 (32)	0.81 (0.63–1.05)	
III–IV	4793 (68)	0.83 (0.72–0.95)	
eGFR			0.70
≥90 mL/min/1.73 m^2	464 (7)	0.77 (0.46–1.30)	
60–89 mL/min/1.73 m^2	2826 (40)	0.89 (0.71–1.11)	
30–59 mL/min/1.73 m^2	3189 (45)	0.78 (0.65–0.94)	
<30 mL/min/1.73 m^2 or dialysis	611 (9)	0.86 (0.63–1.17)	
Ischemic heart disease			0.56
No	1887 (27)	0.78 (0.58–1.05)	
Yes	5203 (73)	0.84 (0.74–0.97)	



The cohort included 7090 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association.

Appendix Figure 5. **Associations between CRT-D versus ICD therapy alone and all-cause readmission in the within-hospital propensity-matched cohort, by patient characteristic.**

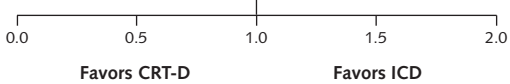
Subgroup	Patients, *n* (%)	CRT-D vs. ICD Hazard Ratio (99% CI)	*P* Value
Age			
65–79 y	5430 (77)	0.86 (0.79–0.94)	0.81
≥80 y	1660 (23)	0.88 (0.76–1.02)	
Sex			0.63
Men	5107 (72)	0.87 (0.80–0.95)	
Women	1983 (28)	0.84 (0.73–0.97)	
Race			0.42
White	6326 (89)	0.86 (0.80–0.93)	
Black	531 (7)	0.98 (0.76–1.26)	
Other/unknown	233 (3)	0.81 (0.54–1.21)	
LBBB/QRS duration			0.113
LBBB/QRS >150 ms	1913 (27)	0.79 (0.68–0.92)	
LBBB/QRS of 120–149 ms	1857 (26)	0.87 (0.76–1.00)	
No LBBB/QRS >150 ms	1120 (16)	0.83 (0.69–1.00)	
No LBBB/QRS of 120–149 ms	2200 (31)	0.95 (0.83–1.09)	
Atrial fibrillation			0.91
No	4825 (68)	0.87 (0.80–0.95)	
Yes	2265 (32)	0.86 (0.76–0.98)	
NYHA functional class			0.053
I–II	2297 (32)	0.93 (0.82–1.06)	
III–IV	4793 (68)	0.83 (0.76–0.91)	
eGFR			0.75
≥90 mL/min/1.73 m^2	464 (7)	0.84 (0.62–1.14)	
60–89 mL/min/1.73 m^2	2826 (40)	0.89 (0.79–1.01)	
30–59 mL/min/1.73 m^2	3189 (45)	0.85 (0.76–0.94)	
<30 mL/min/1.73 m^2 or dialysis	611 (9)	0.82 (0.65–1.04)	
Ischemic heart disease			0.66
No	1887 (27)	0.89 (0.76–1.04)	
Yes	5203 (73)	0.86 (0.79–0.94)	



The cohort included 7090 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association.

Appendix Figure 6. **Associations between CRT-D versus ICD therapy alone and cardiovascular readmission in the within-hospital propensity-matched cohort, by patient characteristic.**

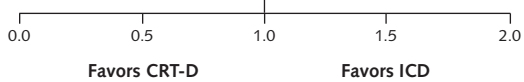
Subgroup	Patients, *n* (%)	CRT-D vs. ICD Hazard Ratio (99% CI)	*P* Value
Age			
65–79 y	5430 (77)	0.80 (0.72–0.89)	0.83
≥80 y	1660 (23)	0.81 (0.68–0.97)	
Sex			0.166
Men	5107 (72)	0.83 (0.75–0.91)	
Women	1983 (28)	0.74 (0.62–0.88)	
Race			0.96
White	6326 (89)	0.81 (0.73–0.88)	
Black	531 (7)	0.78 (0.58–1.06)	
Other/unknown	233 (3)	0.79 (0.48–1.29)	
LBBB/QRS duration			0.004
LBBB/QRS >150 ms	1913 (27)	0.70 (0.58–0.84)	
LBBB/QRS of 120–149 ms	1857 (26)	0.74 (0.62–0.88)	
No LBBB/QRS >150 ms	1120 (16)	0.81 (0.64–1.03)	
No LBBB/QRS of 120–149 ms	2200 (31)	0.96 (0.82–1.11)	
Atrial fibrillation			0.029
No	4825 (68)	0.76 (0.68–0.85)	
Yes	2265 (32)	0.90 (0.77–1.04)	
NYHA functional class			0.115
I–II	2297 (32)	0.87 (0.74–1.02)	
III–IV	4793 (68)	0.77 (0.70–0.86)	
eGFR			0.83
≥90 mL/min/1.73 m^2	464 (7)	0.80 (0.54–1.18)	
60–89 mL/min/1.73 m^2	2826 (40)	0.78 (0.67–0.90)	
30–59 mL/min/1.73 m^2	3189 (45)	0.83 (0.73–0.94)	
<30 mL/min/1.73 m^2 or dialysis	611 (9)	0.76 (0.58–1.00)	
Ischemic heart disease			0.56
No	1887 (27)	0.78 (0.64–0.95)	
Yes	5203 (73)	0.82 (0.74–0.90)	



The cohort included 7090 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association.

Appendix Figure 7. **Associations between CRT-D versus ICD therapy alone and heart failure readmission in the within-hospital propensity-matched cohort, by patient characteristic.**

Subgroup	Patients, *n* (%)	CRT-D vs. ICD Hazard Ratio (99% CI)	*P* Value
Age			
65–79 y	5430 (77)	0.81 (0.70–0.93)	0.37
≥80 y	1660 (23)	0.73 (0.57–0.93)	
Sex			0.002
Men	5107 (72)	0.85 (0.74–0.99)	
Women	1983 (28)	0.61 (0.49–0.77)	
Race			0.49
White	6326 (89)	0.79 (0.69–0.90)	
Black	531 (7)	0.68 (0.47–0.99)	
Other/unknown	233 (3)	0.96 (0.47–1.95)	
LBBB/QRS duration			0.006
LBBB/QRS >150 ms	1913 (27)	0.63 (0.50–0.81)	
LBBB/QRS of 120–149 ms	1857 (26)	0.70 (0.55–0.89)	
No LBBB/QRS >150 ms	1120 (16)	0.82 (0.60–1.13)	
No LBBB/QRS of 120–149 ms	2200 (31)	0.96 (0.78–1.19)	
Atrial fibrillation			0.43
No	4825 (68)	0.76 (0.65–0.90)	
Yes	2265 (32)	0.83 (0.68–1.00)	
NYHA functional class			0.92
I–II	2297 (32)	0.79 (0.62–1.00)	
III–IV	4793 (68)	0.78 (0.68–0.89)	
eGFR			0.97
≥90 mL/min/1.73 m^2	464 (7)	0.82 (0.49–1.40)	
60–89 mL/min/1.73 m^2	2826 (40)	0.77 (0.62–0.97)	
30–59 mL/min/1.73 m^2	3189 (45)	0.78 (0.66–0.93)	
<30 mL/min/1.73 m^2 or dialysis	611 (9)	0.74 (0.52–1.07)	
Ischemic heart disease			0.38
No	1887 (27)	0.73 (0.56–0.94)	
Yes	5203 (73)	0.80 (0.70–0.92)	



The cohort included 7090 patients. CRT-D = cardiac resynchronization therapy with a defibrillator; eGFR = estimated glomerular filtration rate; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; NYHA = New York Heart Association.