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Complications and Mortality Following CRT-D Versus ICD Implants in Older Medicare Beneficiaries With Heart Failure

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ABSTRACT

OBJECTIVES We sought to assess the comparative effectiveness of cardiac resynchronization therapy (CRT) with defibrillator (CRT-D) over implantable cardioverter-defibrillator (ICD) alone in older Medicare patients with heart failure with reduced ejection fraction (HFrEF).

BACKGROUND Despite growing numbers of older patients with HFrEF, the benefits of CRT in this group are largely unknown.

METHODS A cohort of fee-for-service Medicare beneficiaries ≥65 years of age with HFrEF and enrolled in Medicare Part D who underwent CRT-D or ICD implantation from January 2008 to August 2015 was identified. Beneficiaries were divided by age (65-74, 75-84, and 85+ years), and outcomes were compared between the CRT-D and ICD groups after inverse probability weighting.

RESULTS Compared with the ICD group, the CRT-D group was older and more likely to be White, be female, and have left bundle branch block. After weighting, overall complications were high across age and device groups (14%-20%). The 1-year mortality was high across all groups. In the 2 oldest age strata, the hazard of death was lower in the CRT-D group (HR: 0.90; 95% CI: 0.86-0.95 and HR: 0.81; 95% CI: 0.72-0.90, respectively; $P < 0.001$); the hazard of heart failure hospitalization was lower for CRT-D vs ICD in the 85+ years age group (HR: 0.82; 95% CI: 0.74-0.92; $P < 0.001$).

CONCLUSIONS In older Medicare beneficiaries undergoing ICD with or without CRT, complications and 1-year mortality were high. Compared with ICD alone, CRT-D was associated with a lower hazard of mortality in patients ≥74 years of age and lower hazard of HF hospitalization in those ≥85 years of age. These findings support the use of CRT in eligible older patients undergoing ICD implantation. (J Am Coll Cardiol HF 2021;■:■–■) © 2021 by the American College of Cardiology Foundation.

Heart failure (HF) remains a fast-growing cardiovascular disease affecting the Medicare population in large numbers (1,2). Increasingly, HF is managed as a chronic disease, in part because of the incremental improvements achieved with medical and device-based therapies. Despite the large proportion of older patients with HF, clinical trials designed to assess HF interventions rarely include an adequate number of older patients (≥75 years of age) to support well-powered subgroup analysis (3,4).

Cardiac resynchronization therapy (CRT) is one device-based therapy that contributes meaningfully to improvements in the treatment of HF (5,6). CRT can be offered to eligible patients with or without the addition of defibrillator therapy such that patients who qualify based on an increased risk of sudden cardiac death would get CRT with defibrillator

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ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy

CRT-D = cardiac resynchronization therapy with defibrillator

HF = heart failure

ICD = implantable cardioverter-defibrillator

LBBB = left bundle branch block

NCDR = National Cardiovascular Data Registry

NYHA = New York Heart Association

(CRT-D). At times, the response to CRT can be dramatic, resulting in improvements in structural, functional, and quality of life endpoints as well as HF events and death above and beyond those attributable to defibrillator therapy (5,6). Some smaller, nonrandomized studies from mostly single centers suggest that CRT may be associated with these same improvements in a population of older patients with HF (7). Robust multicenter data on older patients are lacking, however. In addition, complications related to CRT implant are likely to differ in an older population, and these risks should be considered as part of a comprehensive evaluation of CRT candidacy in the context of increased competing risks of death inherent to an older population (8-10).

To address these unanswered questions in the absence of randomized data, we examined a population of Medicare beneficiaries with systolic HF undergoing CRT implantation. With an implantable cardioverter-defibrillator (ICD) as the comparator, we compared outcomes in patients undergoing CRT-D implantation to understand the associated risks and benefits of adding CRT in older Medicare beneficiaries.

METHODS

PATIENT COHORT. We identified a population of fee-for-service Medicare beneficiaries with a diagnosis of HF with reduced ejection fraction who are U.S. citizens and at least 65 years of age, as previously described (11). This included limiting the cohort to patients with a prior HF hospitalization event to improve the specificity of the HF diagnosis, as previously reported (11-13). We also limited the cohort to those beneficiaries enrolled in Medicare Part D such that the final cohort was an approximately 20% sample. From this cohort, we further limited the sample to beneficiaries undergoing implantation of an ICD, CRT, or both between January 2008 and August 2015 based on the methodology described by Hatfield et al (14), but device implantation could not occur during the index HF hospitalization. The

TABLE 1 Patient Characteristics by Device Type and Age Group Before Inverse Probability Weighting

	65-74 y		75-84 y		85+ y	
	CRT-D (n = 2,968)	ICD (n = 3,143)	CRT-D (n = 3,568)	ICD (n = 2,929)	CRT-D (n = 739)	ICD (n = 582)
Female	34.4	33.7	37.1	38.2	39.6	35.4
Non-White	14.1	19.2	11.2	16.6	9.61	17.0
Dialysis dependent	[a]	[a]	[a]	[a]	[a]	[a]
CHF primary diagnosis within year prior	61.8	53.3	61.9	51.8	63.3	49.5
Age at implant, y	70.53	70.36	79.13	79.01	87.22	87.13
Ischemic heart disease	80.2	83.3	81.6	82.2	80.5	83.2
Atrial fibrillation	46.2	38.3	51.9	46.9	55.3	54.1
Left bundle branch block	55.2	13.3	54.3	16.6	53.6	20.6
Valvular disease	38.7	36.6	42.0	39.4	44.5	43.0
Peripheral vascular disease	26.1	28.7	26.6	28.5	31.7	31.8
Hypertension	89.8	81.2	91.8	90.9	90.4	93.0
Other neurologic disorders	8.02	8.62	9.30	9.59	7.85	11.2
Chronic lung disease	45.2	47.1	41.4	40.5	33.2	34.7
Diabetes	58.0	56.9	50.1	47.9	39.1	37.1
Renal failure	38.9	36.0	42.6	37.9	45.1	41.2
Obesity	15.4	14.4	8.63	8.64	2.35	2.75
Weight loss	4.99	5.47	5.75	5.91	4.87	5.67
Fluid and electrolyte disorders	38.6	37.3	36.9	35.7	37.8	36.8
Depression	10.0	9.13	8.77	6.86	7.85	8.08
BB fill in prior 90 d	80.9	80.1	77.2	78.2	73.7	75.6
ACE inhibitor/ARB fill in prior 90 d	68.5	68.6	63.2	65.8	60.2	61.2
MRA fill in prior 90 d	32.4	27.9	28.3	25.7	21.1	18.0

Values are % unless noted otherwise. [a]Suppressed because of low numbers.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; BB = beta blocker; CRT-D = cardiac resynchronization therapy with defibrillator; ICD = implantable cardioverter-defibrillator; MRA = mineralocorticoid receptor blocker.

TABLE 2 Patient Characteristics by Device Type and Age Group After Inverse Probability Weighting

	65-74 y			75-84 y			85+ y		
	CRT-D (n = 2,968)	ICD (n = 3,143)	Standard difference	CRT-D (n = 3,568)	ICD (n = 2,929)	Standard difference	CRT-D (n = 739)	ICD (n = 582)	Standard difference
Female	34.4	33.9	-0.011	37.1	36.6	-0.011	39.6	39.0	-0.023
Non-White	14.1	13.7	-0.012	11.2	10.8	-0.015	9.61	9.44	-0.019
Dialysis dependent	[a]	[a]	0.006	[a]	[a]	-0.004	[a]	[a]	-0.006
CHF primary diagnosis within year prior	61.8	63.2	0.030	61.9	62.5	0.013	63.3	66.8	0.073
Ischemic heart disease	80.2	82.5	0.059	81.6	80.8	-0.021	80.5	83.2	0.069
Atrial fibrillation	46.2	49.7	0.069	51.9	54.4	0.050	55.3	55.4	0.001
Left bundle branch block	55.2	56.7	0.030	54.3	55.4	0.022	53.6	55.4	0.037
Valvular disease	38.7	40.1	0.029	42.0	43.0	0.020	44.5	42.9	-0.033
Peripheral vascular disease	26.1	24.5	-0.036	26.6	27.5	0.019	31.7	31.5	-0.004
Hypertension	89.8	90.8	0.035	91.8	92.1	0.013	90.4	90.1	-0.008
Other neurologic disorders	8.02	8.27	0.009	9.30	10.1	0.025	7.85	7.10	-0.028
Chronic lung disease	45.2	45.7	0.010	41.4	41.9	0.010	33.2	36.2	0.064
Diabetes	58.0	60.5	0.051	50.1	50.0	0.000	39.1	40.2	0.021
Renal failure	38.9	39.9	0.020	42.6	44.3	0.034	45.1	46.0	0.019
Obesity	15.4	16.2	0.023	8.63	8.10	-0.019	3.25	3.41	0.009
Weight loss	4.99	4.87	-0.005	5.75	5.88	0.006	4.87	5.66	0.035
Fluid and electrolyte disorders	38.6	41.4	0.056	36.9	36.3	-0.013	37.8	37.7	-0.001
Depression	10.0	8.89	-0.038	8.77	8.21	-0.020	7.85	7.22	-0.024
BB fill in prior 90 d	80.9	80.5	0.011	77.2	76.0	0.014	73.7	69.8	0.013
ACE inhibitor/ARB fill in prior 90 d	68.5	69.0	0.003	63.2	63.9	0.021	60.2	60.8	-0.045
MRA fill in prior 90 d	32.4	32.5	-0.011	28.3	29.2	-0.028	21.1	19.3	-0.088

Values are %. [a]Suppressed because of low numbers.
CHF = congestive heart failure; other abbreviations as in Table 1.

primary cohort was not limited to those with left bundle branch block (LBBB) because of the expectation that this would inadvertently exclude many CRT-eligible patients because of undercoding and because there are various ways of qualifying for CRT without LBBB (eg, HF with pacing indication and anticipated high burden of pacing regardless of QRS morphology or duration) (15). In addition, patients who otherwise met the administrative definition of CRT eligibility (ie, HF plus LBBB) who did not undergo CRT implantation were likely to be fundamentally different, thus biasing results toward CRT. We then divided beneficiaries into age groups: 65-74 years, 75-84 years, and 85+ years.

The group of beneficiaries not undergoing ICD implantation (ie, CRT only) were expected to be different from beneficiaries undergoing ICD implant (with or without CRT) in ways that would not be well represented in the claims data. Therefore, this group was excluded from comparative analyses. This investigation was approved by the Dartmouth-Hitchcock Medical Center Institutional Review Board.

OUTCOMES. The primary outcome of interest was all-cause survival. Date of death was obtained through December 2018 from the Medicare Master Beneficiary Summary File.

Secondary outcomes included HF hospitalization and device-related complications. Complications of interest included predischarge death, bleeding, pneumothorax, pericardial tamponade, infection, vascular complication requiring intervention, upper extremity thrombosis, pulmonary embolism, and mechanical complication. These were derived from International Classification of Diseases-Ninth and -10th Revision codes. If the relevant diagnosis code appeared within 30 days of the device implant code, it was considered reasonably likely to be related to the device implant procedure, with the exception of mechanical complications, for which a 90-day window was applied. Diagnosis codes used to identify complications are reported in Supplemental Table 1. HF hospitalizations were identified based on inpatient hospitalization with a primary relevant diagnosis code (Supplemental Table 1).

STATISTICAL ANALYSIS. We compared patient characteristics based on age and device groups with the chi-square test, and summary statistics are reported as percentages. For medications of interest,

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TABLE 3 Complications by Device Implant Group and Age After Inverse Probability Weighting

	65-74 y			75-84 y			85+ y		
Complication[a]	CRT-D (n = 2,968)	ICD (n = 3,143)	*P* Value	CRT-D (n = 3,568)	ICD (n = 2,929)	*P* Value	CRT-D (n = 739)	ICD (n = 582)	*P* Value
Bleeding	5.42	4.85	0.312	6.53	5.99	0.345	7.44	8.11	0.631
Pneumothorax	2.19	2.18	0.986	2.94	2.61	0.387	2.17	5.41	0.001
Any complication	15.0	15.1	0.860	16.8	14.2	0.002	16.8	19.6	0.154

Values are % unless noted otherwise. [a]Outcomes suppressed because of low numbers: predischarge death, pericardial tamponade, infection, upper extremity thrombosis, pulmonary embolism, mechanical complication, and vascular complication requiring intervention; these were included in "any complication."
Abbreviations as in Table 1.

beneficiaries were identified as taking the medication if there was a prescription filled within 90 days of the procedure. Significant differences between ICD groups with and without CRT were expected in this nonrandomized sample. As a result, we used inverse probability of treatment weighting to balance the CRT-D and ICD groups within each age class with respect to numerous clinical and demographic characteristics, listed in **Tables 1 and 2**. Logistic regression models were used within each category to estimate the probability of treatment (ie, receiving CRT-D), and subjects were weighted by the inverse of these estimated probabilities (16). All reported outcomes and model results incorporate these weights.

In the weighted groups, we compared risk of death overall and by device type and age group using a Cox proportional hazards model and summarized in Kaplan-Meier survival curves. Risk of HF hospitalization was estimated using similar methods with censoring at the time of death.

The cohort of patients identified as having an LBBB was expected to be a relative fraction of the overall cohort and not completely reflective of those patients who qualify for CRT, so the cohort was not limited in this way for the primary analyses. However, because of the importance of this factor, sensitivity analyses were planned and performed in the subgroup of beneficiaries.

RESULTS

BASELINE CHARACTERISTICS. Before weighting, compared with the ICD groups, the CRT-D patients were more likely to be female and White and were slightly older on average (**Table 1**). There were some significant differences in the frequency of medical comorbidities between groups, especially regarding renal failure, atrial fibrillation, and LBBB, all of which were more common in the CRT-D groups. Rates of guideline-directed medical therapy declined with age but were similar between device groups for beta blockers and angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, angiotensin receptor-neprilysin inhibitor; CRT-D patients were more likely to be prescribed a mineralocorticoid receptor antagonist. Inverse probability weighting was successful in balancing these groups (**Table 2**).

DEVICE-RELATED COMPLICATIONS. In the weighted cohort, overall device-related complications were relatively frequent, occurring in 14.3% to 20% of patients, depending on age and device type; the rate generally increased with age (**Table 3**). The highest risk of complication occurred in patients undergoing ICD implant who were 85 years of age or older, and the lowest-risk group was the group of patients 65-74 years of age undergoing CRT-D implant. Bleeding was the most common complication, occurring in 5% to 8% of patients, depending on age and device complexity. Most individual complications, however, occurred too infrequently to report because of Center for Medicare and Medicaid Services suppression rules, which limit the ability to report outcomes in small groups to reduce the risk of inadvertent patient identification.

HF HOSPITALIZATION. For the endpoint of HF hospitalization, there was no difference associated with device type for patients in the 2 younger age strata (65-74 and 75-84 years) (HR: 0.95; 95% CI: 0.90-1.00 and HR: 1.00; 95% CI: 0.95-1.05, respectively; $P > 0.05$ for both). For the oldest age stratum, 85+ years, there was a reduction in the hazard of HF hospitalization associated with CRT-D versus ICD (HR: 0.82; 95% CI: 0.74-0.92; $P < 0.001$) (**Table 4**). When examined over time in a Kaplan-Meier survival analysis within age strata, a significant difference in HF hospitalization was observed in the 85+ age group ($P < 0.01$) (**Figure 1**).

MORTALITY. In the weighted cohorts, mortality was high at 90 days and 1 year, and mortality increased with age. By the end of 1 year, 18% to 33% of patients from each age cohort and device type had died. In contrast to procedure-related complications, the 90-day mortality within age groups was higher in the ICD-only group compared with the CRT-D group (Table 5). The 1-year mortality was similar between CRT-D and ICD patients in the youngest age groups (17.5% vs 18.4%, respectively) but was lower in the CRT-D group in the 2 older age strata (20.7% vs 23.8% and 25.7% vs 32.2%, respectively; $P < 0.001$ for both).

The Cox proportional hazards model estimating the HR of death demonstrated that the hazard of death was similar in the CRT-D group compared with the ICD-only group within the 65-74 years stratum (HR: 0.96; 95% CI: 0.90-1.02; $P = 0.171$), but there was a lower hazard of mortality associated with CRT-D in the 2 older strata: HR: 0.90; 95% CI: 0.86-0.95 (75-84 years) and HR: 0.81; 95% CI: 0.72-0.90 (85+ years); $P < 0.001$ for both (Table 4). When examined over time in a Kaplan-Meier survival analysis within age strata, a similar pattern was seen with a significant difference in survival associated with CRT-D in the 75-84 years and 85+ years age groups ($P < 0.001$) (Central Illustration).

SENSITIVITY ANALYSES. The analyses were repeated in the subgroup of beneficiaries with LBBB. As expected, the subgroup of patients with LBBB was small, with just over 100 subjects in each of the CRT-D and ICD groups in the oldest age stratum. Otherwise, the LBBB subgroup was similar to the overall cohort on measured characteristics and comorbidities, except the LBBB cohort was more likely to be female (>40% in all groups compared with <40% in the overall cohort). Despite a smaller sample, weighting was successful within age groups. Complications were not meaningfully different in the LBBB subgroup compared with the overall cohort. There was a significant mortality benefit associated with CRT-D over ICD alone in each age group with LBBB including the youngest stratum (65-74 years), and the associated benefit was greater than that seen in the overall cohort (Supplemental Table 2). Furthermore, the associated benefits with regard to mortality and HF hospitalization increased with age.

TABLE 4 HR Of Death And Heart Failure Hospitalization Of CRT-D Versus ICD By Age Stratum After Inverse Probability Weighting

Event	Age, y	n	HR, CRT-D vs ICD	P Value	95% CI Lower Limit	95% CI Upper Limit
Death	65-74	6,111	0.96	0.171	0.90	1.02
	75-84	6,497	0.90	<0.001	0.86	0.95
	85+	1,321	0.81	<0.001	0.72	0.90
Heart failure hospitalization	65-74	6,111	0.95	0.052	0.90	1.00
	75-84	6,497	1.00	0.937	0.95	1.05
	85+	1,321	0.82	<0.001	0.74	0.92

Abbreviations as in Table 1.

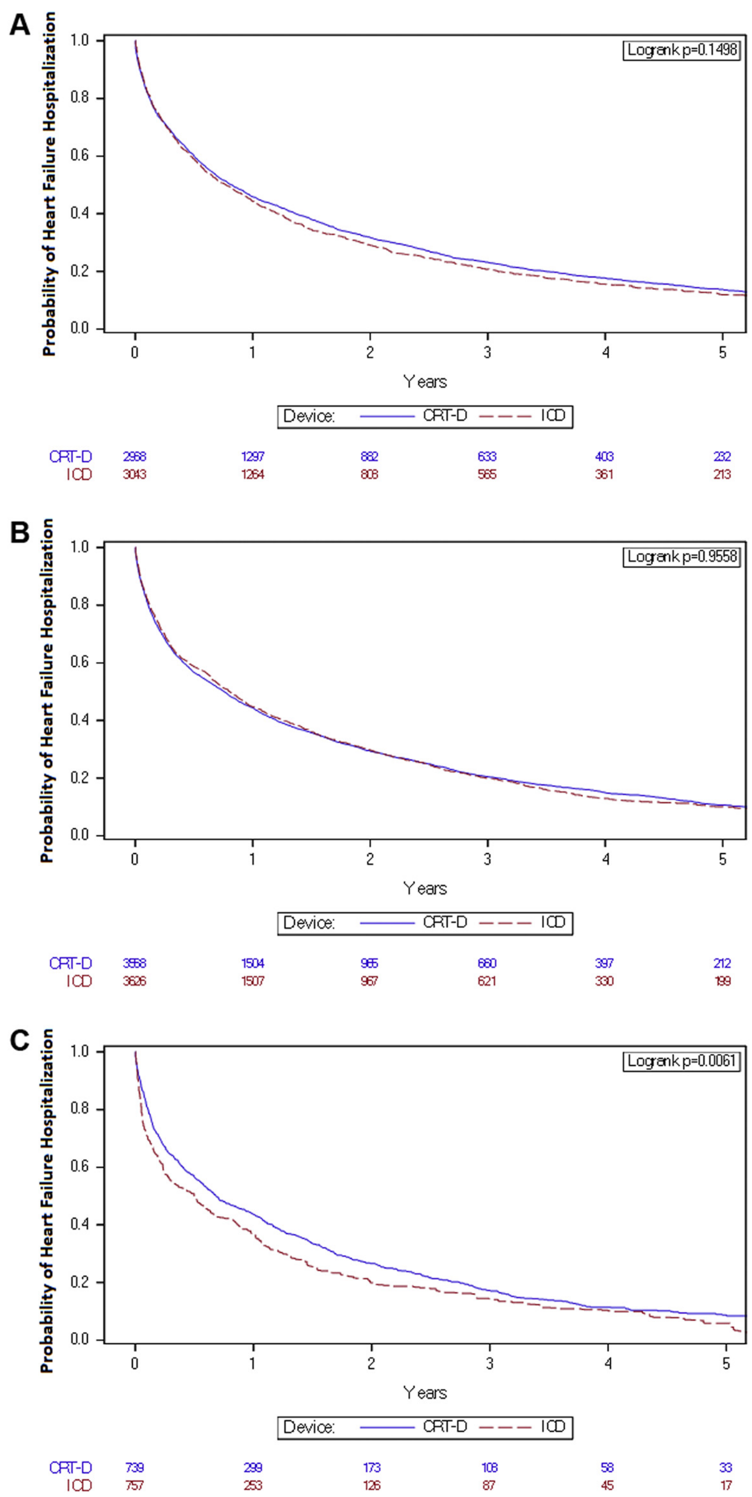
DISCUSSION

Despite the transition of the population of patients with HF to one that is older and more comorbid, evidence that supports that most HF therapies were derived in younger, healthier patients. Evidence that supports the ICD and CRT for eligible subjects largely comes from high-quality randomized controlled trials, but the average age of randomized subjects was 64-66 years, and the enrollment of older patients was limited (5,6,17,18). This evidence is reflected in age-agnostic guidelines by relevant professional societies (19). Indeed, the benefit of CRT in older patients has been identified as a major gap in knowledge and as a priority for future research (20). Limited single-center and retrospective investigations in older patients with HF have suggested that these devices have been applied broadly to older populations with promising results (10,21). A meta-analysis of these smaller observational studies by our group recently suggested that there was similar improvement in left ventricular ejection fraction in older patients receiving CRT compared with younger patients (<70 years) and no meaningful difference in procedure-related complications (7). However, evidence suggests that CRT remains underused in all groups (22,23), especially older populations (24,25). Some solutions for addressing underuse of CRT in eligible patients have been proposed by authoritative sources (22) for which additional evidence supporting the benefit of the therapy, like that presented here, is additive.

Thus, in the absence of randomized data, we sought to evaluate the comparative safety and effectiveness of CRT-D vs ICD only in a population of older patients with HF. This investigation has 3 main findings. First, at baseline, there are important differences among patients undergoing ICD placement with or without CRT in a real-world Medicare cohort. Second, complications and mortality following implant procedures are high across all device and age groups. Third, there was improved survival associated with CRT-D over ICD alone in the 2 older age strata: 75-84 years and 85+ years; when limited to those with LBBB, this association was extended to the youngest group and was amplified across all groups.

With an average age of 76 years, our population was significantly older than patients included in clinical trials of CRT, and had many comorbidities, including high rates of ischemic heart disease, atrial

FIGURE 1 **Comparative Heart Failure Hospitalization Following CRT-D Versus ICD by Age Group**



Kaplan-Meier survival without heart failure hospitalization in weighted cohorts of elderly patients based on CRT-D versus ICD implant: **(A)** 65-74 **(B)** 75-84 and **(C)** 85+ years of age. CRT-D = cardiac resynchronization therapy with defibrillator; ICD = implantable cardioverter-defibrillator.

TABLE 5 Mortality By Device Implant Group And Age After Inverse Probability Weighting

	65-74 y			75-84 y			85+ y		
	CRT-D	ICD	*P* Value	CRT-D	ICD	*P* Value	CRT-D	ICD	*P* Value
Death within 90 d	5.76	7.39	0.01092	7.01	9.37	0.00026	8.80	15.7	0.00005
Death within 1 y	17.5	18.4	0.36612	20.7	23.8	0.00152	24.8	33.4	0.00024

Values are % unless noted otherwise.
Abbreviations as in Table 1.

fibrillation, and diabetes. In the comparison of interest, CRT-D vs ICD, some characteristics of the CRT-D group reflect eligibility criteria for CRT (eg, greater burden of LBBB) or those criteria associated with positive response to CRT, including female sex and less ischemic heart disease. For these reasons and because we could not independently evaluate beneficiary candidacy for CRT (eg, New York Heart Association [NYHA] functional class), inverse probability weighting was used to balance these differences between groups to better understand the differences in clinical outcomes associated with CRT over ICD alone.

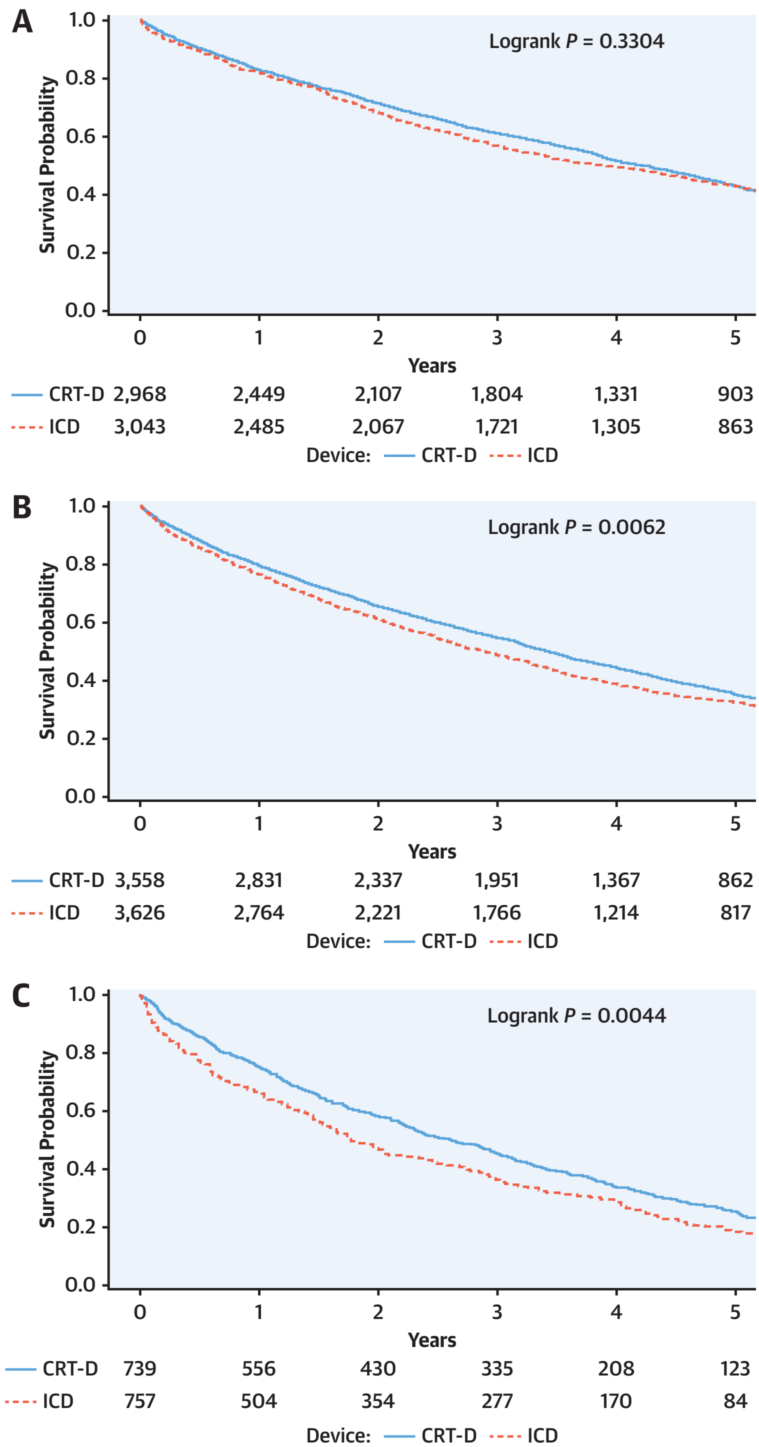
In this clinical cohort of Medicare beneficiaries, we found that there was relatively high mortality. In prior reports from the National Cardiovascular Data Registry (NCDR) for ICDs, which was nearly universally inclusive of ICD procedures in Medicare patients until February 2018, the 1-year mortality rate for CRT-D patients ranged from 8.3% to 11.7%, compared with 20% in our analysis despite a similar average age (26,27). In another NCDR ICD Registry study, the 1-year mortality in a population of older patients with an ICD ranged from 9.9% in the youngest group (65-69 years) to 18.9% in the oldest group (≥80 years) (28). In comparison, our study represents a selected subgroup based on a validated claims-based diagnosis of HF with reduced ejection fraction including an admission for HF as part of the inclusion criteria (11). This narrowed the analysis to a group with higher expected mortality than "all-comer" Medicare beneficiaries with HF (29). Nonetheless, the 1-year mortality rate in the oldest CRT subgroup was nearly 25%, which closely approximates the mortality rate seen in a population with advanced HF undergoing ICD implantation, including patients with NYHA class IV symptoms, recent inotropic support, left ventricular assist device in situ, or current listing for orthotopic heart transplant (30).

Reasons for the high mortality rate are unknown because cause of death was not available, but it likely reflects significant competing nonarrhythmic mortality risk, which is difficult to measure from claims data. This is problematic because relevant professional guidelines consistently recommend ICD (with or without CRT) only when life expectancy is at least 1 year (19), but estimating survival is notoriously unreliable and is commonly based on clinical gestalt. This is particularly true in the oldest patients, for whom clinical trial data are absent and estimates of mortality from observational studies are widely variable (7,31,32). Estimating competing mortality risk may be exacerbated by a dispersed medical system in which the severity and burden of noncardiovascular disease in a specific patient may be difficult or impossible for an implanting physician to ascertain.

However, reassuringly, CRT-D was associated with significantly improved survival over ICD alone in the 2 oldest age groups, with the greatest difference in survival associated with CRT-D seen in the oldest group (85+ years); in the youngest age stratum, patients receiving CRT-D and ICD had a similar hazard of death. When examined by age strata, there was an increasing proportion of ICD patients with LBBB (13.3%, 16.6%, and 20.6%, respectively), suggesting that there may have been an increasing association between patient selection and CRT-D candidacy based on factors not well captured in claims data, like frailty. Reassuringly, in a sensitivity analysis limited to the cohort of patients with LBBB, there was significant mortality and HF hospitalization benefit associated with CRT-D over ICD alone in all groups (Supplemental Table 2). One hypothesis for the discrepancy in outcomes for the youngest age group seen between the overall cohort and the LBBB subgroup is that patient selection for CRT in younger groups may be more inclusive rather than less, so only with the more restrictive LBBB cohort was a benefit seen in this group. As a corollary, this may also mean that patient selection for CRT is particularly restrictive in older patients and that more liberal patient selection may bring significant benefits to more older patients.

The 1-year life expectancy requirement for ICD eligibility highlighted in professional guidelines is partially based on balancing the expected benefit with competing risks of death, which may include

CENTRAL ILLUSTRATION Comparative Survival Following Cardiac Resynchronization Therapy with Defibrillation Versus ICD by Age Group



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Kaplan-Meier survival in weighted cohorts of elderly patients based on cardiac resynchronization therapy with defibrillation versus ICD implant: **(A)** 65-74 **(B)** 75-84 and **(C)** 85+ years of age. ICD = implantable cardioverter-defibrillator.

procedural complications. Using claims data, it is not possible to assess how concern about complications did or did not affect referral decisions or implant decisions by patients or operators. In our cohort, procedural complications were common, occurring in about 15% of patients, with increasing complications associated with increasing age and device complexity. The most common complication was bleeding, and the second most common was pneumothorax. Rates of complication seen in this cohort far exceeded rates previously reported from the NCDR ICD Registry, which have generally reported 1-year complication rates around 1% to 4% using similar claims-based definitions (26,27). As noted regarding the mortality findings, the cohorts in this analysis represent an older and highly comorbid group, which may account for this discrepancy.

STUDY LIMITATIONS. First, analysis cohorts were not limited to those with LBBB, so although many patients without LBBB may qualify for CRT, there are likely patients included in both the CRT-D and ICD groups who do not meet guideline criteria for CRT; sensitivity analyses, however, demonstrate consistent findings in the subgroup of patients with LBBB. Second, device groups were not randomized, so despite attempts to measure and account for residual confounding, it cannot be excluded as an explanation for these findings. For example, the frequency of LBBB in the ICD group increased with age, suggesting that otherwise-CRT-eligible patients may not have received CRT more frequently with increasing age because of nonmeasurable variables like perceived procedural risk. Importantly, unmeasured variables include institutional variability, patient and operator preferences, and some components of CRT candidacy, including NYHA functional class, left ventricular ejection fraction, and QRS duration. Patients who decline device implant or who are eligible but never offered device implant are not represented in this analysis. Our analysis was limited to Medicare Fee-for-Service patients with prior HF hospitalization, so although this data set encompasses the majority of Americans over age 65 years, it is not all inclusive, and results may not be generalizable to other populations (eg, Medicare managed care or patients with HF without prior HF hospitalization). Finally, this investigation included implant procedures through August 2015, so both International Classification of Diseases-Ninth and -10th Revision codes were identified to measure 90-day procedural complications and hospitalization, and these codes have not been formally validated. More work is needed to validate International Classification of Diseases-10th Revision codes for contemporary claims-based investigations. Finally, treatment effects cannot be completely derived from these data.

CONCLUSIONS

This large, real-world comparative effectiveness analysis of CRT-D vs ICD in Medicare patients with HF, reduced ejection fraction, and prior HF hospitalization addresses persistent questions related to the expected benefits of CRT over ICD in older patients, which likely contributes to underuse of CRT in this group. These findings demonstrate significant improvements in mortality and HF hospitalization associated with CRT-D in the oldest patients. Overall mortality and complications attributable to device implantation are higher than previously reported, which, in part, likely reflects an evolving HF population that is increasingly older and comorbid. As such, the inclusion of older patients in future randomized clinical trials of HF interventions would improve understanding of therapies in this growing population.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The benefits of CRT over ICD alone established in clinical trials have been extrapolated to older patients with HF. Because the population of patients with HF includes more older patients, understanding the benefits and risks of these therapies is critically important. In a real-world cohort of Medicare beneficiaries, CRT was associated with benefit over ICD alone in patients ≥75 years of age with regard to mortality and HF hospitalization. Therefore, in eligible patients, CRT-D should be considered over ICD alone regardless of age.

TRANSLATIONAL OUTLOOK: In the absence of dedicated clinical trials for older patients with HF with reduced ejection fraction, the clinical benefit of HF interventions, like CRT, must be extrapolated from clinical trial populations, which tend to be younger. In this analysis, CRT was associated with mortality benefit in the oldest Medicare beneficiaries. Future work is needed to understand the interaction between medical therapy and device therapy in HF, both of which continue to evolve. Furthermore, the inclusion of older patients in future clinical studies of HF therapies will help clarify risks and benefits in this unique population.

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KEY WORDS cardiac resynchronization therapy, heart failure, implantable defibrillator, mortality

APPENDIX For supplemental tables, please see the online version of this paper.