Comparison of Mortality and Readmission in Non-Ischemic Versus Ischemic Cardiomyopathy After Implantable Cardioverter-Defibrillator Implantation

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Data is lacking on the contemporary risk of death and readmission following implantable cardioverter-defibrillator (ICD) implantation in patients with non-ischemic cardiomyopathies (NICM) compared with ischemic cardiomyopathies (ICM) in a large nationally representative cohort. We performed a retrospective cohort study using the National Cardiovascular Data Registry ICD Registry linked with Medicare claims from April 1, 2010 to December 31, 2013. We established a cohort of NICM and ICM patients with a left ventricular ejection fraction ≤35% who received a de novo, primary prevention ICD. We compared mortality and readmission using Kaplan-Meier curves and Cox proportional hazard regressions models. We also evaluated temporal trends in mortality. In 31,044 NICM and 68,458 ICM patients with a median follow up of 2.4 years, 1-year mortality was significantly higher in ICM patients (12.3%) compared with NICM (7.9%, p < 0.001). The higher mortality in ICM patients remained significant after adjustment for covariates (hazard ratio [HR] 1.40; 95% confidence interval [CI] 1.36 to 1.45), and was consistent in subgroup analyses. These findings were consistent across the duration of the study. ICM patients were also significantly more likely to be readmitted for all causes (adjusted HR 1.15, CI 1.12 to 1.18) and for heart failure (adjusted HR 1.25, CI 1.21 to 1.31). In conclusion, the risks of mortality and hospital readmission after primary prevention ICD implantation were significantly higher in patients with ICM compared with NICM which was consistent across all patient subgroups tested and over the duration of the study. **(Am J Cardiol 2020;133:116−125)**

Patients with a reduced left ventricular fraction (LVEF) are at increased risk of sudden cardiac death.[1,2] Implantable cardioverter defibrillators (ICDs) for primary prevention reduce all-cause mortality in patients with ischemic cardiomyopathy (ICM),[3−6] but data supporting their use for patients with non-ischemic cardiomyopathy (NICM) are less robust. Of 6 ICD trials that reported their outcomes separately for patients with NICM, only Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) showed lower all-cause mortality in the NICM patient subgroup.[3,7−11] However, meta-analysis of randomized trials suggest that NICM patients receiving an ICD have a significant reduction in all-cause mortality and sudden cardiac death compared with medically treated controls.[12−15] The meta-analyses combined data from trials that enrolled in the 1990s to early 2000s, before the use of more contemporary medical therapies. Contemporary observational studies have shown mixed results regarding outcomes after ICD implantation in patients with NICM[16−18] and about half of clinicians surveyed in European countries have changed their practices for primary prevention ICD implantation as a result of the DANISH trial, adopting a more conservative approach to implantation.[19] In this study we evaluated real-world rates of death and readmission after primary prevention ICD implantation overall and for patients with ICM compared with patients with NICM, using contemporary data from the National Cardiovascular Data Registry (NCDR) ICD Registry. We also evaluated temporal trends in mortality after ICD implantation.

Methods

The NCDR ICD Registry was established in 2005 by the American College of Cardiology and Heart Rhythm Society to improve the safety, treatment and patterns of care for

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This work was supported by the American College of Cardiology (ACC) Foundation's National Cardiovascular Data Registry (NCDR). The views expressed represent those of the author(s) and do not necessarily represent the official views of the NCDR or its associated professional societies (www.ncdr.com).

See page 124 for disclosure information.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2020.07.035

patients receiving ICD implantation.[20] In 2006, the Centers for Medicare and Medicaid Services (CMS) mandated reporting on all Medicare patients receiving primary prevention ICDs through February 15, 2018. Most participating hospitals (90%) also reported data from additional patient populations during this period, such as those receiving ICDs for secondary prevention and those ensured by other payers.[20] The NCDR ICD Registry data collection methods have previously been described and validated.[21–23] The Yale University Human Investigation Committee approved the present analysis with waiver of informed consent.

All CMS Medicare fee-for-service beneficiaries with a LVEF ≤35% who had a de-novo implantation of a primary prevention ICD or cardiac resynchronization therapy defibrillator device between April 1, 2010 and December 31, 2013 were included in the study (Figure 1). This allowed for a minimum 1 year follow-up as CMS linkage data was available through December 31, 2014. The NCDR ICD Registry V2.1 data collection form was used. NICM was defined as reduced ejection fraction without a diagnosis of ischemic disease or previous coronary revascularization. ICM was defined as a diagnosis of ischemic heart disease, with 1 epicardial artery with at least 70% stenosis by angiography. Patients <65 years of age were excluded, as were patients who had a syndrome with increased risk of sudden death (long QT syndrome, short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, idiopathic ventricular tachycardia/fibrillation), or who had structural abnormalities (cardiac amyloidosis, congenital cardiac defect, Chagas disease, giant cell myocarditis, hypertrophic cardiomyopathy, left ventricular aneurysm, left ventricular noncompaction, arrhythmogenic right ventricular dysplasia, and cardiac sarcoidosis). Patients on dialysis and those with a documented life expectancy <1 year were excluded, as well as patients with an epicardial system or a subcutaneous ICD.

The primary outcome was all-cause mortality after ICD implantation. The secondary outcomes were all-cause readmission and heart failure readmission after ICD implantation. Outcomes were obtained from NCDR ICD Registry data linkage to CMS files for readmission (inpatient institutional claims) and Master Beneficiary Summary file for death. This file obtains death information from the

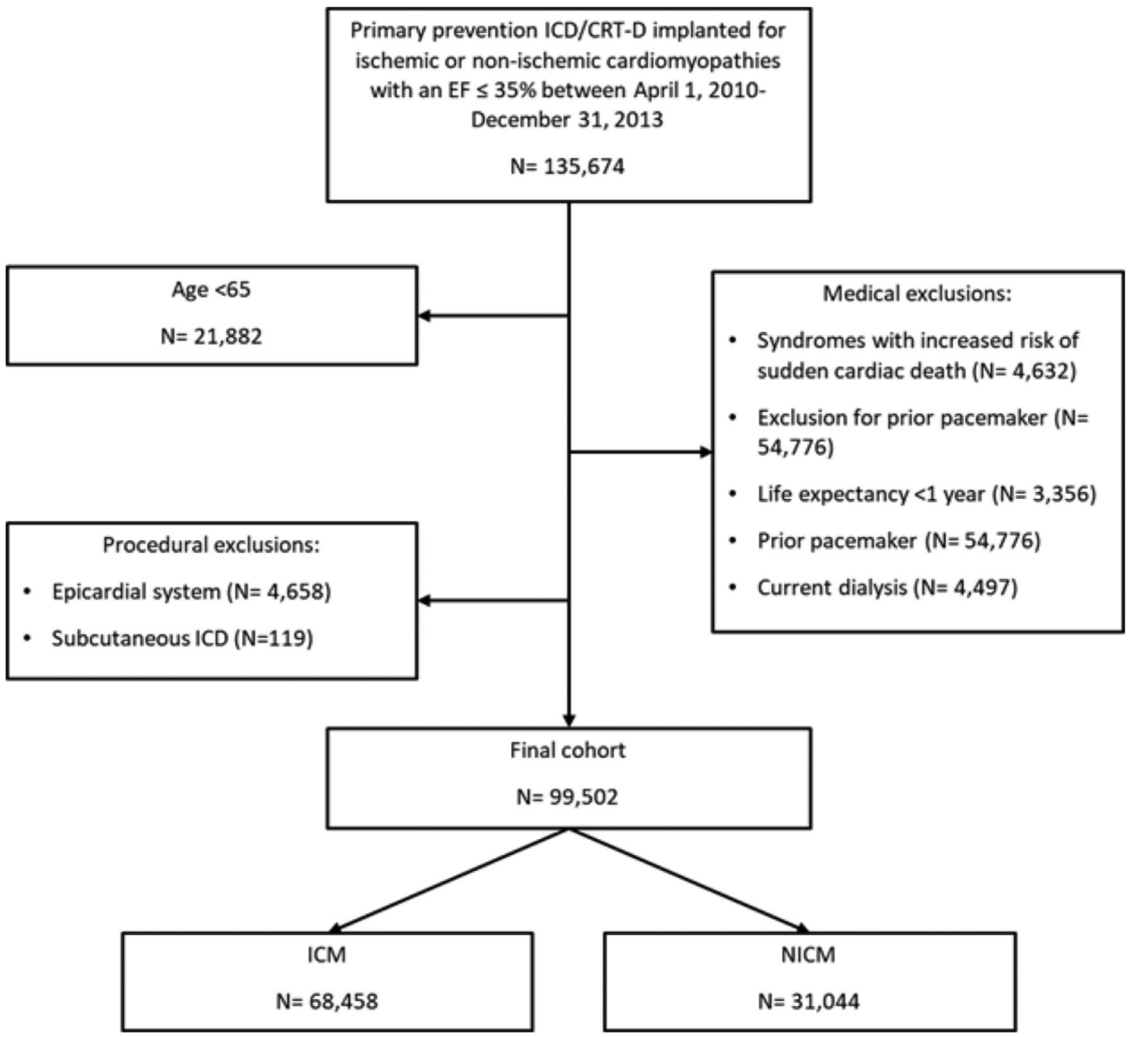

Figure 1. Study population selection flow diagram.

Medicare Common Working File, online date of death edits, and benefit information used to administer the Medicare program collected from the Railroad Retirement Board and the Social Security Administration. Only 0.1% of deaths were excluded due to lack of verified date of death.

Statistical analyses were performed using SAS v9.4 (SAS institute; Cary, NC). Baseline characteristics were compared using Pearson's Chi Square for categorical data and Wilcoxon rank-sum test for continuous data, and reported as number (%) and median (interquartile range or mean [standard deviation]), with associated p-values. We also evaluated periprocedureal event rates with sensitivity analyses to account for the presence or absence or cardiac resynchronization therapy devices.

For the primary outcome of death, the Kaplan-Meier method was used to calculate the actuarial event-free rates and differences were compared using the log-rank test. Event free rates, adjusted for baseline differences in patient and device characteristics at implantation, were assessed using a Cox-proportional hazards regression model. For secondary outcomes of hospital admissions, cumulative incidence functions were calculated and tested using Gray's test. Fine-Gray models accounting for competing risks of death were utilized to estimate subdistribution hazard ratios (HR) for ICM versus NICM groups. Patients were censored at the end of the available follow-up period for mortality analyses, and at death or the end of Medicare fee-for-service enrollment for readmissions. The HR or subdistribution HR and the corresponding 95% confidence interval (CI) for all-cause death, all-cause readmission, and heart failure readmission were calculated. Clinically relevant covariates were evaluated and all covariates with an unadjusted HR p-value <0.2 were included in multivariable Cox-proportional hazards regression models. Clinically significant subgroup analyses were also evaluated. Missing values were imputed before modeling. Dichotomous (yes/no) variables were assumed to be no, whereas all other variables were imputed using fully conditional specification.[24] For our analysis all variables were missing < 1% of the time.

We performed a time series analysis to compare temporal trends in 1-year mortality in patients with NICM compared with ICM. 1-year mortality was plotted as a function of calendar time of device implantation. To evaluate for a difference in trends of death in NICM compared with ICM over time, we tested whether the slopes of the 2 groups were significantly different using a likelihood ratio test.

Results

A total of 135,674 patients who had an ICD implantation performed between April 1, 2010 and December 31, 2013, met inclusion criteria. Following exclusions, 99,502 patients (31,044 NICM and 68,458 ICM) remained, (Figure 1). The average age of the overall cohort was 75 years, 27% were female**,** the average LVEF was 26%, and most patients had New York Heart Association Class III (57%) heart failure (Table 1). Almost half of all patients (49%) had cardiac resynchronization therapy. The use of guideline-directed medical therapy was high; 78% were on an ACE-inhibitor or angiotensin receptor blocker and 90% were on a beta-blocker. Patients with NICM were more likely to be female, non-Hispanic black, have New York Heart Association class III symptoms, LVEF <30%, QRS duration ≥140 ms, atrial fibrillation and more likely to be treated with cardiac resynchronization therapy, digoxin, and warfarin (Table 1). Patients with NICM were less likely to be white and to have cerebrovascular disease, diabetes mellitus,and hypertension, and were less likely to be treated with lipid lowering agents, platelet inhibitors, and nitroglycerin (Table 1).

Peri-procedural events were uncommon overall (1.6%), and had somewhat different patterns for ICM and NICM patients (Table 2). The overall periprocedural death rate was 0.35% (n = 350), and lower in the NICM group (0.19% vs 0.43%, p = <0.0001). Although cardiac arrest was significantly lower for patients with NICM (0.14% vs 0.25%, p = 0.0003), rates of cardiac perforation (0.18% vs 0.06%), and coronary venous dissection (0.31% vs 0.14%) were all significantly higher in those with NICM (p < 0.0001), although absolute differences were modest. When stratified by cardiac resynchronization therapy, the results were consistent with the overall findings, although some were no longer statistically significant (Supplementary Table 1).

Over a median follow-up of 2.4 years (intequartile range 1.5 to 3.4 years) unadjusted mortality after ICD implantation was substantially higher in our cohort than reported in earlier primary prevention ICD trials (Supplementary Table 2). Mortality was significantly higher after ICD implant in ICM patients compared with NICM patients over 5 years of follow-up (Figure 2). One-year all-cause mortality was 12.3% for patients with ICM, compared with 7.9% for patients with NICM (p < 0.001). Mortality remained higher after adjustment for other covariates, with an adjusted HR of 1.40 (CI: 1.36 to 1.45) that was consistent in all subgroups (Table 3). There was no significant change in mortality over time, either in patients with ICM or in patients with NICM (Figure 3).

The unadjusted rate of readmission was significantly higher for patients with ICM compared with NICM (Figure 4**, Panel A**). The thirty-day unadjusted readmission rate for patients with ICM was 8.1% (CI: 7.9 to 8.3) compared with 7.1% (CI: 6.8 to 7.4) in patients with NICM (p < .0001). After adjusting for significant covariates, and accounting for competing risk of death, patients with ICM had a significantly higher rate of all-cause readmission over the entire follow-up period (adjusted HR 1.15, CI: 1.12 to 1.18) (Table 4). This pattern was consistent across all subgroups, and significant in most subgroups. Heart failure readmissions were also higher in patients with ICM. (Figure 4**, Panel B**), with an adjusted HR of 1.15 (CI: 1.21 to 1.31) (Table 5). Heart failure readmissions were higher across all subgroups, and significantly so in most subgroups (Table 5).

Discussion

In this large, U.S. national cohort of patients with a LVEF ≤35% who received a primary prevention ICD or cardiac resynchronization therapy defibrillator device, all-cause mortality and readmission were significantly higher in patients with ICM compared with NICM. The higher mortality for patients with ICM remained significant after accounting for differences in patient characteristics, and was consistent in all subgroups. The 1-year risk of death

Table 1
Baseline characteristics of patients implanted with an implantable cardioverter-defibrillator overall and comparing those with non-ischemic cardiomyopathy and ischemic cardiomyopathy

Characteristic	Overall 99,502 (100.0%)	NICM 31,044 (31.2%)	ICM 68,458 (68.8%)	p-value
Age (years)				<0.0001
Mean (SD)	74.50 (6.3%)	74.05 (6.2%)	74.70 (6.3%)	
65-75	57,353 (57.6%)	18,729 (60.3%)	38,624 (56.4%)	
> 75	42,149 (42.4%)	12,315 (39.7%)	29,834 (43.6%)	
Gender				<0.0001
Male	72,687 (73.1%)	17,721(57.1%)	54,966 (80.3%)	
Female	26,815 (27.0%)	13,323 (42.9%)	13,492 (19.7%)	
Race				<0.0001
Non-Hispanic white	83,311 (83.7%)	23,910 (77.0%)	59,401 (86.8%)	
Non-Hispanic black	9,278 (9.3%)	4,892 (15.8%)	4,386 (6.4%)	
Hispanic	5,043 (5.1%)	1,716 (5.5%)	3,327 (4.9%)	
Other	1,870 (1.9%)	526 (1.7%)	1,344 (2.0%)	
Heart failure				<0.0001
No	10,159 (10.2%)	2,149 (6.9%)	8,010 (11.7%)	
Yes for < 9months	26,687 (26.8%)	9,163 (29.5%)	17,524 (25.6%)	
Yes for ≥ 9 months	62,620 (63.0%)	19,724 (63.6%)	42,896 (62.7%)	
NYHA Class				<0.0001
I	6,313 (6.4%)	1,302 (4.2%)	5,011 (7.3%)	
II	33,131 (33.4%)	9,255 (29.9%)	23,876 (35.0%)	
III	56,743 (57.2%)	19,430 (62.7%)	37,313 (54.7%)	
IV	3,073 (3.1%)	1,009 (3.3%)	2,064 (3.0%)	
Syncope	13,154 (13.2%)	4,004 (12.9%)	9,150 (13.4%)	0.04
Family history of sudden death	2,408 (2.4%)	707 (2.3%)	1,701 (2.5%)	0.05
Atrial fibrillation/flutter	39,853 (40.1%)	13,360 (43.1%)	26,493 (38.7%)	<0.0001
Ventricular tachycardia	23,953 (24.1%)	6,803 (21.9%)	17,150 (25.1%)	<0.0001
Cerebrovascular disease	17,818 (17.9%)	3,782 (12.2%)	14,036 (20.5%)	<0.0001
Diabetes mellitus	41,150 (41.4%)	10,242 (33.0%)	30,908 (45.2)	<0.0001
Chronic lung disease	24,023 (24.2%)	6,798 (21.9%)	17,225 (25.2%)	<0.0001
Sleep apnea	11,354 (11.4%)	3,765 (12.2%)	7,589 (11.1%)	<0.0001
Hypertension	84,318 (84.8%)	24,735 (79.8%)	59,583 (87.1%)	<0.0001
Left ventricular ejection fraction				<0.0001
Mean (SD)	25.73 (6.3)	24.87 (6.5)	26.12 (6.2)	
< 30%	58,540 (58.8%)	19,825 (63.9%)	38,715 (56.6%)	
≥30%	40,962 (41.2%)	11,219 (36.1%)	29,743 (43.5%)	
QRS duration				<0.0001
QRS duration (among nonventricular paced) - Median (IQR)	125 (102-152)	136 (106-158)	121 (102-149)	
Ventricular paced rhythms only	10,279 (10.3%)	3,637 (11.7%)	6,642 (9.7%)	
< 140	55,311 (55.7%)	14,501 (46.8%)	40,810 (59.7%)	
≥ 140	33,799 (34.0%)	12,869 (41.5%)	20,930 (30.6%)	
Chronic kidney disease stage				<0.0001
Normal - GFR > 90	10,444 (10.6%)	3,599 (11.7%)	6,845 (10.1%)	
2 - GFR 60−89	36,675 (37.2%)	12,382 (40.2%)	24,293 (35.8%)	
3 - GFR 30−59	44,683 (45.3%)	13,094 (42.6%)	31,589 (46.5%)	
4 - GFR 15−29	6,344 (6.4%)	1,556 (5.1%)	4,788 (7.1%)	
5 - GFR <15	541 (0.6%)	145 (0.5%)	396 (0.6%)	
Cardiac resynchronization therapy	49,003 (49.3%)	18,651 (60.2%)	30,352 (44.4%)	<0.0001
Discharge medications				
Ace-inhibitor or angiotensin receptor blocker	76,895 (77.6%)	24,937 (80.5%)	51,958 (76.2%)	<0.0001
Aspirin	72,652 (73.3%)	17,706 (57.2%)	54,946 (80.6%)	<0.0001
Beta blockers	89,622 (90.4%)	28,047 (90.6%)	61,575 (90.4%)	0.32
Lipid lowering agents	74,272 (74.9%)	17,255 (55.7%)	57,017 (83.7%)	<0.0001
Platelet aggregation inhibitors	26,878 (27.1%)	1,250 (4.0%)	25,628 (37.6%)	<0.0001
Calcium channel blockers	8,590 (8.7%)	2,551 (8.2%)	6,039 (8.9%)	0.001
Digoxin	17,717 (17.9%)	6,846 (22.1%)	10,871 (16.0%)	<0.0001
Diuretic	67,926 (68.5%)	22,264 (71.9%)	45,662 (67.0%)	<0.0001
Hydralazine	4,957 (5.0%)	1,545 (5.0%)	3,412 (5.0%)	0.90
Long acting nitroglycerin	13,249 (13.4%)	1,977 (6.4%)	11,272 (16.5%)	<0.0001
Warfarin	29,810 (30.1%)	10,612 (34.3%)	19,198 (28.2%)	<0.0001
Amiodarone	13,399 (13.5%)	3,776 (12.2%)	9,623 (14.1%)	<0.0001
Other antiarrhythmic	2,706 (2.7%)	832 (2.7%)	1,874 (2.8%)	0.57

Abbreviations: GFR = glomerular filtration rate; ICM = ischemic cardiomyopathy; IQR = interquartile range; NICM = non-ischemic cardiomyopathy; NYHA = New York Heart Association; SD = standard deviation.

Table 2
Periprocedural adverse events after implantable cardioverter-defibrillator implantation among patients overall and comparing those with non-ischemic cardiomyopathy and ischemic cardiomyopathy

	Overall		NICM		ICM		
	# of Events	Rate (IQR)	# of Events	Rate (IQR)	# of Events	Rate (IQR)	p-value
Any Event	1,615	1.62 (1.55−1.70)	549	1.77 (1.62−1.92)	1,066	1.56 (1.47−1.65)	0.014
Death	350	0.35 (0.32−0.39)	59	0.19 (0.14−0.25)	291	0.43 (0.38−0.48)	<0.0001
Cardiac arrest	214	0.22 (0.19−0.25)	42	0.14 (0.10−0.18)	172	0.25 (0.22−0.29)	0.0003
Myocardial infarction	25	0.03 (0.02−0.04)	4	0.01 (0.00−0.03)	21	0.03 (0.02−0.05)	0.10
Cardiac perforation	95	0.10 (0.08−0.12)	55	0.18 (0.13−0.23)	40	0.06 (0.04−0.08)	<0.0001
Coronary venous dissection	190	0.19 (0.16−0.22)	97	0.31 (0.25−0.38)	93	0.14 (0.11−0.17)	<0.0001
Tamponade	118	0.12 (0.10−0.14)	62	0.20 (0.15−0.26)	56	0.08 (0.06−0.11)	<0.0001
Stroke/transient ischemic attack	57	0.06 (0.04−0.07)	16	0.05 (0.03−0.08)	41	0.06 (0.04−0.08)	0.61
Hematoma	326	0.33 (0.29−0.37)	88	0.28 (0.23−0.35)	238	0.35 (0.30−0.39)	0.10
Infection requiring antibiotics	62	0.06 (0.05−0.08)	18	0.06 (0.03−0.09)	44	0.06 (0.05−0.09)	0.71
Hemothorax	31	0.03 (0.02−0.04)	10	0.03 (0.02−0.06)	21	0.03 (0.02−0.05)	0.90
Pneumothorax	407	0.41 (0.37−0.45)	182	0.59 (0.50−0.68)	225	0.33 (0.29−0.37)	<0.0001
Urgent cardiac surgery	28	0.03 (0.02−0.04)	11	0.04 (0.02−0.06)	17	0.02 (0.01−0.04)	0.36

Abbreviations: ICM = ischemic cardiomyopathy; IQR = interquartile range; NICM = non-ischemic cardiomyopathy.

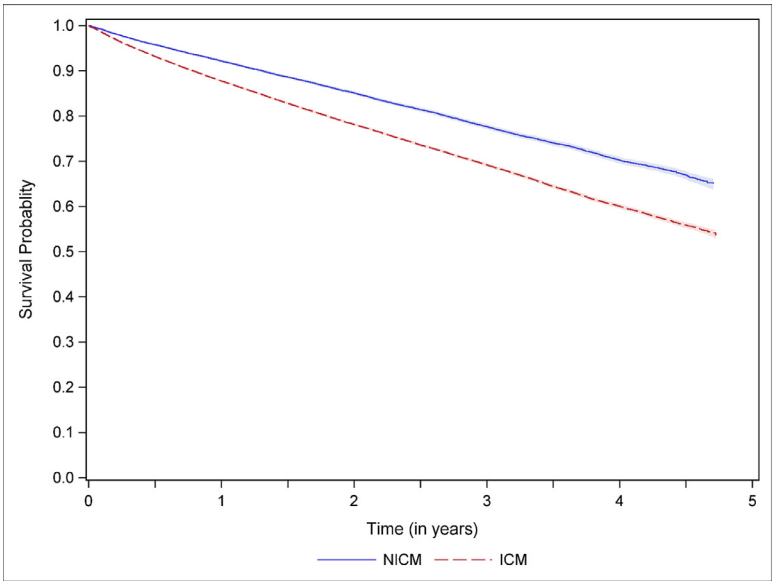

Figure 2. Kaplan meier curve comparing mortality after implantable cardioverter-defibrillator placement in ischemic cardiomyopathy (dashed red line) and nonischemic cardiomyopathy patients (solid blue line).

was unchanged over the duration of the study, and remained consistently higher in patients with ICM.

The overall mortality rates in this contemporary real-world national registry study were higher than those reported for all the major ICD clinical trials and this finding was consistent in both those with ICM and NICM (Supplementary Table 2). The 1-year mortality of 12.3% in the ICM cohort was higher than MADIT-II (9%),[6] and the 3-year mortality in our study (31%) approached the 5-year mortality in the ICM group of the SCD-HeFT trial (36%).[3] The 1-year mortality rates in the NICM cohort of our study were also higher than in the DEFINITE (7.9% vs 2.6%),[7] AMIOVERT (7.9% vs 4%), and DANISH trials (7.9% vs 2.9%),[10] but similar to the CAT trial (7.9% vs 8%).[9] The higher mortality in our registry study is likely due to the selection of lower risk patients for clinical trials, whereas patients in this real-world cohort of Medicare beneficiaries had more advanced age, higher rates of co-morbidities, and more symptomatic heart failure.[25]

The DANISH trial found no significant improvement in all-cause mortality from ICD implantation in patients with NICM, although sudden cardiac death was significantly reduced.[10] Meta-analyses of randomized trials suggest that ICDs do reduce mortality and sudden cardiac death compared with medically treatment in those with NICM.[12−15] DANISH was much more recent than the trials included in the meta-analyses, and the use of contemporary medical therapies with overall lower risk of all-cause and sudden death may account for the differing results. Although our study study does not directly evaluate the effectiveness of ICDs in NICM compared with ICM, our data showing that

Table 3
Mortality over 2.5-year median follow-up after implantable cardioverter defibrillator implantation in patients with ischemic cardiomyopathy compared with non-ischemic cardiomyopathy as the reference group

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Adjusted HR p-value
All Patients	1.48 (1.44−1.52)	1.40 (1.36−1.45)	< 0.0001
Subgroup			
Age (years)			
65−75	1.52 (1.46−1.58)	1.50 (1.43−1.57)	< 0.0001
>75	1.40 (1.35−1.45)	1.32 (1.26−1.38)	< 0.0001
Gender			
Male	1.35 (1.30−1.39)	1.36 (1.31−1.41)	< 0.0001
Female	1.74 (1.66−1.83)	1.43 (1.35−1.52)	< 0.0001
Race			
Non-Hispanic white	1.55 (1.50−1.60)	1.44 (1.39−1.50)	< 0.0001
Non-Hispanic black	1.25 (1.16−1.35)	1.20 (1.09−1.31)	0.0001
Hispanic	1.53 (1.35−1.73)	1.39 (1.21−1.60)	< 0.0001
Other	1.45 (1.17−1.8)	1.37 (1.07−1.76)	0.0124
Cardiac resynchronization therapy			
Yes	1.26 (1.21−1.32)	1.32 (1.26−1.38)	< 0.0001
No	1.72 (1.66−1.79)	1.45 (1.39−1.51)	< 0.0001
NYHA Class			
I	1.40 (1.20−1.62)	1.38 (1.16−1.63)	0.0002
II	1.51 (1.43−1.6)	1.48 (1.39−1.59)	< 0.0001
III	1.58 (1.53−1.63)	1.38 (1.33−1.44)	< 0.0001
IV	1.47 (1.3−1.65)	1.36 (1.18−1.56)	< 0.0001
Left ventricular ejection fraction			
< 30%	1.52 (1.47−1.58)	1.38 (1.33−1.44)	< 0.0001
≥ 30%	1.49 (1.42−1.57)	1.43 (1.35−1.51)	< 0.0001
Antiarrhythmic medications			
Amiodarone	1.33 (1.25−1.43)	1.28 (1.18−1.38)	< 0.0001
Other antiarrhythmic	1.66 (1.39−1.98)	1.54 (1.25−1.89)	< 0.0001
Heart failure status			
No	1.48 (1.32−1.67)	1.56 (1.37−1.79)	< 0.0001
Yes for < 9 months	1.70 (1.61−1.79)	1.53 (1.43−1.63)	< 0.0001
Yes for ≥ 9 months	1.45 (1.40−1.50)	1.34 (1.29−1.40)	< 0.0001

Abbreviations: CI = confidence interval; HR = hazard ratio; NYHA = New York Heart Association.

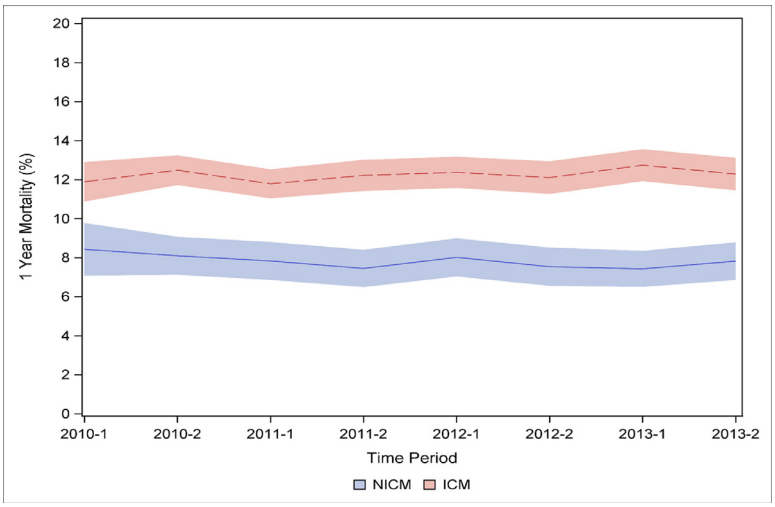

Figure 3. One-year mortality after implantable cardioverter-defibrillator placement in ischemic cardiomyopathy (dashed red line) and nonischemic cardiomyopathy patients (solid blue line).

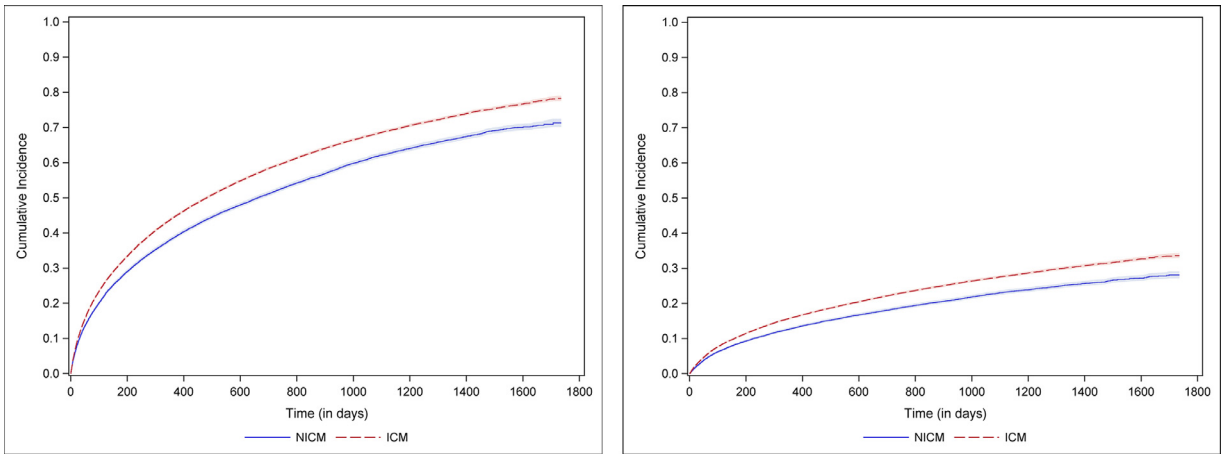

Figure 4. (*A*) All-cause readmission and (*B*) Heart failure readmission after implantable cardioverter-defibrillator placement in ischemic cardiomyopathy (dashed red line) and nonischemic cardiomyopathy patients (solid blue line).

patients with NICM have substantially lower risk of death compared with ICM patients are very consistent with the findings of DANISH.

Previous observational studies evaluating mortality in patients with NICM compared with ICM have shown mixed results. Our results were consistent with those of a recent smaller and more limited study of approximately 5,000 patients (2,181 with NICM and 3,304 with ICM) that found higher mortality in ICM patients that persisted in multivariable analysis (adjusted HR 1.31, CI 1.06 to 1.61, p = 0.01) and after propensity score matching.[17] In contrast, a smaller study of 310 propensity-matched patients (556 with ICM

Table 4
All-cause readmission after implantable cardioverter defibrillator implantation for patients with ischemic cardiomyopathy compared with non-ischemic cardiomyopathy (NICM) overall and according to subgroup, accounting for competing risk of death, with NICM as the reference group

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Adjusted HR p-value
All Patients	1.20 (1.18−1.23)	1.15 (1.12−1.18)	< 0.0001
Subgroup			
Age (years)			
65−75	1.21 (1.18−1.24)	1.18 (1.14−1.22)	< 0.0001
>75	1.17 (1.14−1.21)	1.12 (1.08−1.16)	< 0.0001
Gender			
Male	1.18 (1.15−1.21)	1.13 (1.10−1.17)	< 0.0001
Female	1.37 (1.32−1.42)	1.16 (1.11−1.21)	< 0.0001
Race			
Non-Hispanic white	1.24 (1.21−1.27)	1.16 (1.13−1.2)	< 0.0001
Non-Hispanic black	1.19 (1.12−1.26)	1.10 (1.02−1.18)	0.01
Hispanic	1.21 (1.10−1.33)	1.03 (0.92−1.16)	0.56
Other	1.22 (1.03−1.43)	1.26 (1.03−1.54)	0.022
Cardiac resynchronization therapy			
Yes	1.10 (1.06−1.13)	1.12 (1.08−1.16)	< 0.0001
No	1.31 (1.27−1.34)	1.17 (1.13−1.21)	< 0.0001
New York Heart Association Class			
I	1.10 (0.99−1.21)	1.02 (0.91−1.14)	0.78
II	1.23 (1.18−1.28)	1.20 (1.14−1.26)	< 0.0001
III	1.25 (1.21−1.28)	1.14 (1.11−1.18)	< 0.0001
IV	1.20 (1.08−1.33)	1.13 (0.99−1.28)	0.06
Left ventricular ejection fraction			
< 30%	1.22 (1.18−1.25)	1.15 (1.11−1.18)	< 0.0001
≥ 30%	1.20 (1.16−1.24)	1.16 (1.11−1.20)	< 0.0001
Antiarrhythmic medications			
Amiodarone	1.15 (1.09−1.21)	1.11 (1.05−1.18)	0.0005
Other antiarrhythmic	1.25 (1.11−1.41)	1.22 (1.07−1.40)	0.004
Heart failure status			
No	1.13 (1.05−1.22)	1.12 (1.02−1.22)	0.013
Yes for < 9 months	1.30 (1.25−1.36)	1.22 (1.17−1.28)	< 0.0001
Yes for ≥ 9 months	1.19 (1.16−1.22)	1.13 (1.09−1.16)	< 0.0001

Abbreviations: CI = confidence interval = HR, hazard ratio.

Table 5
Heart failure readmission after implantable cardioverter defibrillator implantation for patients with ischemic cardiomyopathy compared with non-ischemic cardiomyopathy (NICM) overall and according to subgroup, accounting for competing risk of death, with NICM as the reference group

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Adjusted HR p-value
All Patients	1.25 (1.21−1.29)	1.25 (1.21−1.31)	< 0.0001
Subgroup			
Age (years)			
65−75	1.24 (1.18−1.30)	1.28 (1.21−1.36)	< 0.0001
>75	1.23 (1.17−1.29)	1.23 (1.16−1.30)	< 0.0001
Gender			
Male	1.19 (1.14−1.24)	1.21 (1.16−1.27)	< 0.0001
Female	1.51 (1.43−1.6)	1.30 (1.21−1.39)	< 0.0001
Race			
Non-Hispanic white	1.38 (1.33−1.44)	1.31 (1.25−1.37)	< 0.0001
Non-Hispanic black	1.08 (0.99−1.17)	1.09 (0.99−1.21)	0.09
Hispanic	1.31 (1.13−1.51)	1.20 (1.01−1.44)	0.04
Other	1.08 (0.84−1.38)	1.10 (0.81−1.49)	0.54
Cardiac resynchronization therapy			
Yes	1.02 (0.97−1.07)	1.15 (1.08−1.22)	< 0.0001
No	1.48 (1.42−1.55)	1.33 (1.26−1.40)	< 0.0001
New York Heart Association Class			
I	1.24 (1.03−1.50)	1.20 (0.96−1.51)	0.11
II	1.19 (1.12−1.27)	1.25 (1.15−1.35)	< 0.0001
III	1.35 (1.29−1.40)	1.27 (1.21−1.33)	< 0.0001
IV	1.19 (1.02−1.39)	1.15 (0.95−1.38)	0.15
Left ventricular ejection fraction			
< 30%	1.25 (1.2−1.30)	1.22 (1.17−1.29)	< 0.0001
≥ 30%	1.32 (1.24−1.4)	1.32 (1.23−1.42)	< 0.0001
Antiarrhythmic medications			
Amiodarone	1.17 (1.08−1.28)	1.21 (1.10−1.33)	0.0001
Other antiarrhythmic	1.48 (1.19−1.83)	1.52 (1.19−1.95)	0.0008
Heart failure status			
No	1.15 (0.99−1.33)	1.17 (0.98−1.39)	0.08
Yes for < 9 months	1.49 (1.39−1.59)	1.42 (1.30−1.54)	< 0.0001
Yes for ≥ 9 months	1.21 (1.16−1.26)	1.21 (1.15−1.27)	< 0.0001

Abbreviations: CI = confidence interval; HR = hazard ratio.

and 226 with NICM) found no significant difference in mortality (19.4% vs 20%, p = 0.38),[16] but had low statistical power for modest differences. Our study is larger than these previous studies, including 99,052 patients (68,458 ICM and 31,044 NICM) with greater statistical power to detect differences. Previous studies have shown that patients with ICM remain at substantially increased risk of sudden and all-cause death despite advances in cardiac medical and procedural therapies.[17] We did not have data on cause of death in our study, however Amara et al found that patients with ICM were more likely to die of noncardiovascular causes.[17]

Readmission rates were higher in patients with ICM compared with NICM in our study. These findings are consistent with another recent study which showed that, despite advances in treatment for coronary artery disease, patients with ischemic heart disease are more likely to be readmitted after ICD implantation. That study evaluated over 70,000 patients and showed that the presence of coronary artery disease was associated with a significantly increased risk of readmission after ICD implantation.[26] The overall 30-day readmission rate of 12% in that study was higher than in ours (8.1%), but the overall pattern of higher readmission in ICM patients was similar.

As in any observational cohort study, our findings may have some degree of residual confounding. However, the ICD Registry collects data on most recognized prognostic factors, and our analyses were adjusted for all major clinical risk factors. Our study only included patients 65 years or older with Medicare fee-for-service coverage, which may limit its generalizability to other age groups. This population does, however, represent the majority of primary prevention ICDs implanted in contemporary practice, and the real-world outcomes in our study are more representative than those among very selected clinical trial populations. We also did not have data on rates of appropriate or inappropriate ICD therapies, and therefore can not evaluate any differences between NICM and ICM. Lastly, we did not have a control group of patients without an ICD, and thus cannot directly assess the benefit of ICDs compared with medical therapy. This study is however the largest study to date comparing outcomes after ICD implantation in patients with NICM and ICM and offers important insight into the real-world contemporary risk of mortality and readmission in these groups.

In conclusion, the risk of mortality and readmission after primary prevention ICD implantation in this nationally representative cohort of patients was significantly higher in

patients with ICM compared with NICM and these findings were consistent across multiple patient subgroups and over the duration of the study.

Data Availability Statement

Data are available upon reasonable request.

Author Contributions

Angela Higgins: Conceptualization, methodology, writing-original draft, review and editing, visualization. Jenny Bjerre: Conceptualization, methodology, writing- review and editing. Craig S. Parzynski: Methodology, formal analysis, data curation, writing- review and editing. Karl E. Minges: Methodology, writing- review and editing, project administration. Tariq Ahmad: Writing- review and editing. Nihar R. Desai: Writing- review and editing. Alan Enriquez: Writing- review and editing. Erica S. Spatz: Writing-review and editing. Daniel J. Friedman: Writing- review and editing. Jeptha P. Curtis: Conceptualization, methodology, writing- review and editing, supervision. Mark A. Hlatky: Conceptualization, methodology, writing- review and editing, supervision. James V. Freeman: Conceptualization, methodology, writing- original draft, review and editing, supervision.

Disclosures

Drs. Curtis and Minges and Craig Parzynski receive salary support for analytic services provided to the American College of Cardiology. Dr. Friedman has received: modest educational grants from Boston Scientific, Medtronic, and Abbott; modest research grants from the National Cardiovascular Data Registry, Boston Scientific, Abbott, Medtronic, and Biosense Webster; modest consulting fees from Abbott; salary support via the National Institutes of Health. Dr. Curtis has a contract with the American College of Cardiology for his role as Senior Medical Officer, NCDR; receives funding from the Centers for Medicare & Medicaid Services to develop and maintain performance measures that are used for public reporting; and holds significant equity interest in Medtronic. Dr. Freeman reports modest Consulting/Advisory Board fees from Janssen Pharmaceuticals, Medtronic, Boston Scientific and Biosense Webster. He receives salary/research support from the ACC and the National Heart Lung and Blood Institute. The remaining authors have no disclosures to report.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.07.035.

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