Implantable Cardioverter-Defibrillators in Patients with CKD: A Propensity-Matched Mortality Analysis

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Abstract

Background and objectives Benefits of transvenous implantable cardioverter-defibrillators (ICDs) in prevention of sudden cardiac death among the general population are proven. However, the benefit of ICDs remains unclear in CKD. A propensity-matched analysis was conducted to examine the survival benefits of ICDs placed for primary prevention in those with CKD not on dialysis (eGFR<60 ml/min per 1.73 m^2).

Design, setting, participants, & measurements The Cleveland Clinic CKD registry was utilized to identify individuals who had an echocardiogram at the institution (between 2001 and October 2011). A propensity score of the likelihood of receiving an ICD was developed with the following variables: demographics, comorbid conditions, use of cardioprotective medications, eGFR, left ventricular ejection fraction, and ventricular arrhythmia. One-to-one greedy matching was used with 0.1 caliper width to match patients with and without an ICD. A Cox proportional hazards model was used to examine survival of matched patients with and without an ICD.

Results This study included 1053 ICD patients and 9435 potential controls. Of 1053 ICD patients (60%), 631 were matched to the control group. During a median follow-up of 2.9 years (25th and 75th percentiles, 1.5, 4.7), 578 patients died. After adjusting for covariates, the hazard of mortality among propensity-matched patients was 0.69 (95% confidence interval [95% CI], 0.59 to 0.82) for the ICD group compared with the non-ICD group. A significant interaction was found between ICDs and eGFR (P=0.04). Presence of an ICD was associated with a lower risk of death among those with eGFRs of 45–59 ml/min per 1.73 m^2 (hazard ratio [HR], 0.58; 95% CI, 0.44 to 0.77) and 30–44 ml/min per 1.73 m^2 (HR, 0.65; 95% CI, 0.50 to 0.85), but not among those with eGFRs<30 ml/min per 1.73 m^2 (HR, 0.98; 95% CI, 0.71 to 1.35).

Conclusions Transvenous ICDs placed for primary prevention are associated with a survival benefit in those with stage 3 CKD, but not in those with stage 4 CKD.

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Introduction

CKD is a worldwide public health problem that affects 13.1% of the American population (1). CKD is associated with increased cardiovascular mortality, particularly from sudden cardiac death (2–4). As noted in recent clinical trials, the benefit of implantable cardioverter-defibrillators (ICDs) in primary and secondary prevention of sudden cardiac death is well established in the general population with cardiovascular disease (5–8). The American College of Cardiology/American Heart Association clinical practice guidelines recommend placement of ICDs for secondary prevention in patients in which a reversible cause is not identified, and for primary prevention in patients with heart failure associated with prior myocardial infarction (ejection fraction ≤30%), cardiomyopathy (ejection fraction ≤35%), or intraventricular conduction delay (QRS≥120 milliseconds) (9–11).

Most of the clinical trials studying transvenous ICDs either excluded patients with advanced renal disease or did not report renal function details (12). Thus, evidence exploring the benefits of ICDs in those with nondialysis-dependent CKD remains scarce. Recent studies have shown that patients with an ICD and kidney disease have a higher mortality rate compared with those without kidney disease (13–16). However, the absence of control groups (comprising patients that did not receive an ICD) in most of these studies prevents us from drawing conclusions as to whether ICD therapy confers a survival benefit in patients with nondialysis-dependent CKD. Neither the American College of Cardiology/American Heart Association/Heart Rhythm Society nor the European Society of Cardiology guidelines address the particular indications of ICDs in patients with CKD. Therefore, the purpose of this study is to examine the mortality benefits of transvenous ICD placement in patients with different stages of CKD (eGFR<60 ml/min per 1.73 m^2), an important question that suffers from a striking paucity of data.

Materials and Methods

Study Population

We conducted an analysis using our preexisting electronic health record (EHR)–based CKD registry. The development and validation of our EHR-based CKD registry at Cleveland Clinic were described in detail elsewhere (17). Patients who met the following criteria between January 1, 2005, and September 15, 2009, were considered for inclusion in this analysis: (*1*) had at least one face-to-face outpatient encounter with a Cleveland Clinic health care provider; (*2*) had two eGFR values <60 ml/min per 1.73 m^2, calculated using the CKD Epidemiology Collaboration (CKD-EPI) equation >90 days apart (18); and (*3*) for the ICD group in our current analysis, patients had an ICD implanted for primary prevention between January 1, 2001, and October 31, 2011. During the development of the CKD registry, patients aged <18 years and those who were diagnosed with ESRD needing dialysis or renal transplantation before CKD diagnosis were excluded.

Definitions and Outcome Measures

Renal Function. To calculate eGFR, we applied the CKD-EPI equation to patients in our health system that had two outpatient serum creatinine levels between January 1, 2005, and September 15, 2009. All creatinine measurements were performed by the modified kinetic Jaffe reaction, using a Hitachi D2400 Modular Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN) in our laboratory. All serum creatinine assays were standardized to isotope dilution mass spectrometry. CKD was defined according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines, as follows: stage 3 CKD (eGFR 30–59 ml/min per 1.73 m^2), stage 4 CKD (eGFR 15–29 ml/min per 1.73 m^2), and stage 5 CKD (eGFR<15 ml/min per 1.73 m^2). We further categorized stage 3 into CKD stage 3a (eGFR 45–59 ml/min per 1.73 m^2) and stage 3b (eGFR 30–44 ml/min per 1.73 m^2).

ICD and Left Ventricular Ejection Fraction. We identified patients with International Classification of Diseases, Ninth Revision, codes for ICD in the encounter diagnosis or problem list of the EHR at any time before October 31, 2011. We defined ICD by the codes V45.02 and V53.32. One of the investigators (G.N.) conducted a chart review to confirm the presence of an ICD and to obtain details about the left ventricular ejection fraction as well as the primary indication of the procedure for all patients.

Comorbid Conditions and Laboratory Parameters. Demographic details were extracted from the EHR. Diabetes mellitus, hypertension, coronary artery disease, and other comorbid conditions were defined using prespecified criteria and validated in a previous publication (17). All comorbid conditions were defined at study entry.

Outcome Measures. The primary outcome of interest (all-cause mortality) was ascertained from our EHRs and linkage of our CKD registry with the Social Security Death Index. Patients were followed from their date of study entry (date of second qualifying eGFR or first ICD) until October 31, 2011.

Statistical Analyses

We compared the baseline characteristics of patients with and without an ICD using *t* tests for continuous variables and chi-squared tests for categorical variables. We developed a propensity score of the likelihood of receiving an ICD, utilizing the following variables: age, sex, race, diabetes, hypertension, malignancy, body mass index, coronary artery disease, coronary revascularization, congestive heart failure, ventricular arrhythmia, cerebrovascular disease, eGFR, left ventricular ejection fraction, and use of renin-angiotensin system blockers, statins, and β-blockers. We used one-to-one greedy matching with 0.1 caliper width to match patients with an ICD to those without. We evaluated the resulting matched patients by graphing standardized differences of the variables included in the propensity score before and after the match. We also compared their characteristics with *t* tests for continuous variables and chi-squared tests for categorical ones.

We used a Kaplan–Meier curve to compare the survival of matched patients with and without ICDs at different eGFR intervals (<30 ml/min per 1.73 m^2, 30–44 ml/min per 1.73 m^2, and 45–59 ml/min per 1.73 m^2). We also used unadjusted and adjusted Cox proportional hazard models, and we tested an interaction between the three eGFR intervals and ICDs. We fit an adjusted model including hemoglobin and albumin, which were not included in the propensity match, as well as age and ventricular arrhythmia, which were included in the propensity match but remained slightly imbalanced after matching. We tested an interaction between ICD and eGFR of 45–59 ml/min per 1.73 m^2 versus eGFR of 30–44 ml/min per 1.73 m^2 versus eGFR<30 ml/min per 1.73 m^2. To account for the matched nature of the data, we used the covariance sandwich estimator in the Cox proportional hazards models. For the survival models, patients with no ICD had inception date at second eGFR<60 ml/min per 1.73 m^2. Patients with an ICD had their inception at second eGFR<60 ml/min per 1.73 m^2 or ICD placement, whichever was last. Because patients who had an ICD (before and after development of CKD) were included in the primary analysis, we performed two different sensitivity analyses. In the first sensitivity analysis, we evaluated the associations of ICDs with mortality exclusively among patients who had their ICD placed after second eGFR<60 ml/min per 1.73 m^2, along with their respective controls. In this sensitivity analysis, inception for the ICD group was date of ICD placement. Similarly, we evaluated the associations of ICDs with mortality exclusively among patients who had their ICD placed before second eGFR<60 ml/min per 1.73 m^2 along with their respective controls. In this sensitivity analysis, inception for the ICD group was date of second eGFR<60 ml/min per 1.73 m^2. To evaluate the effect of excluding unmatched patients with an ICD from analysis, we also fit a Cox model on all participants with ICDs and all potential controls while adjusting for age, sex, race, diabetes, hypertension, malignancy, body mass index, coronary artery disease, coronary revascularization, congestive heart failure, ventricular arrhythmia, cerebrovascular disease, eGFR, left ventricular ejection fraction, hemoglobin, albumin, and use of renin-angiotensin system blockers, statins, and β-blockers. In addition, we tested the interaction between ICDs and the three eGFR groups. In a sensitivity analysis, we also fitted a similar model in the unmatched data while excluding all patients with baseline malignancy. Fourteen percent of patients were missing albumin and 7% were missing hemoglobin. Mean value imputation was used in adjusted models while including dummy

indicators for missing data, and complete case analysis was also performed that yielded similar results. In a sensitivity analysis, we censored patients at the time of transitioning to dialysis to ensure that the analysis represents only nondialysis-dependent CKD. All patients who survived until September 15, 2009, (last date United States Renal Data System data were available for our CKD registry) were censored on that date for mortality analyses.

Results

Baseline Characteristics

We included 1053 patients who had an ICD placed for primary prevention (Figure 1). The median time between ICD and the eGFR used in the study was 7 months, with the 25th and 75th percentiles being 1 and 21 months, respectively. We identified 9435 potential controls for those with an ICD. The overall mean age was 71.1±11.4 years. Eighteen percent of patients were black and 32% were women. Table 1 shows patient characteristics before the propensity matching. Patients with an ICD were more likely to be younger, were more likely to be men, and were more likely to have lower ejection fraction, diabetes, congestive heart failure, and coronary artery disease compared with those with no ICD (Table 1). As expected, there was a higher incidence of arrhythmia in the ICD group.

Matching

The logistic model for the propensity score had a c-statistic of 0.97. We were able to match 631 of 1053 patients (60%) with an ICD with 0.1 calipers. After the match, all variables had standardized differences <10%, except age and ventricular arrhythmia, which had a standardized difference of 12% and 11%, respectively (Figure 2). Table 2 displays the characteristics of the matched group.

Outcomes

Among the 1262 matched cases and controls, there were 578 deaths during a median follow-up of 2.9 years (25th and 75th percentiles, 1.5, 4.7). Figure 3 shows a Kaplan–Meier plot of survival by ICD among matched patients with different eGFR categories. After propensity score matching, ICD was associated with significantly lower mortality among those with an eGFR<60 ml/min per 1.73 m^2 in both the unadjusted and adjusted models (Table 3). In the unadjusted model, presence of an ICD was associated with a hazard ratio (HR) of 0.65 (95% confidence interval [95% CI], 0.55 to 0.77). In the adjusted model, presence of an ICD was associated with a HR of 0.69 (95% CI, 0.59 to 0.82). We found a significant interaction (P=0.04) between ICD and an eGFR of 45–59 ml/min per 1.73 m^2 and an eGFR of 30–44 ml/min per 1.73 m^2, in which patients with an ICD and an eGFR within these two intervals had a significantly lower hazard of mortality, with HRs of 0.58 (95% CI, 0.44 to

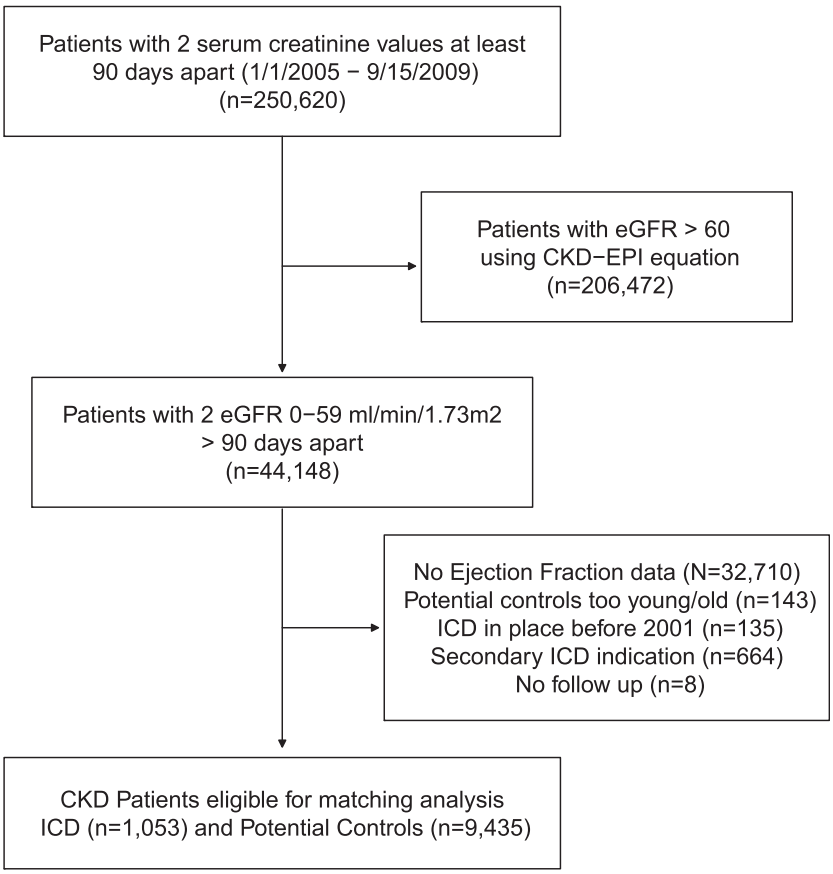

Figure 1. | Flow chart showing how patients were selected for this analysis. CKD-EPI, CKD Epidemiology Collaboration; ICD, implantable cardioverter defibrillator.

Table 1. Patient characteristics by presence of an ICD before propensity match

Factor	Patients (*n*)	Non-ICD Group (*n*=9435)	ICD Group (*n*=1053)	*P* Value
Age (yr)	10,488	72.0±11.7	69.6±11.5	<0.001
Men	10,488	4770 (50.6)	748 (71.0)	<0.001
Black race	10,488	1526 (16.2)	173 (16.4)	0.83
BMI (kg/m^2)	10,182	29.2±6.6	28.9±5.9	0.21
BMI group (kg/m2)	10,488			<0.001
<18.5		129 (1.4)	6 (0.57)	
18.5–24.9		2370 (25.1)	282 (26.8)	
25–29.9		3263 (34.6)	368 (34.9)	
≥30		3372 (35.7)	392 (37.2)	
Missing		301 (3.2)	5 (0.47)	
eGFR (ml/min per 1.73 m^2)	10,488	44.6±12.0	43.5±11.3	0.004
CKD stage, by eGFR (ml/min per 1.73 m^2)	10,488			<0.001
45–59		5408 (57.3)	532 (50.5)	
30–44		2751 (29.2)	374 (35.5)	
15–29		1081 (11.5)	141 (13.4)	
<15		195 (2.1)	6 (0.57)	
Diabetes	10,488	2136 (22.6)	322 (30.6)	<0.001
Hypertension	10,488	8041 (85.2)	802 (76.2)	<0.001
Congestive heart failure	10,488	1349 (14.3)	698 (66.3)	<0.001
Coronary artery disease	10,488	2875 (30.5)	602 (57.2)	<0.001
Cerebrovascular disease	10,488	1165 (12.3)	124 (11.8)	0.59
Peripheral vascular disease	10,488	322 (3.4)	54 (5.1)	0.01
Coronary revascularization	10,488	590 (6.3)	181 (17.2)	<0.001
Ventricular arrhythmia	10,488	41 (0.43)	72 (6.8)	<0.001
Albumin (g/dl)	8967	4.0±0.52	4.1±0.48	0.001
Hemoglobin (g/dl)	9595	12.4±1.9	12.6±1.9	<0.001
Malignancy	10,488	2284 (24.2)	145 (13.8)	<0.001
LVEF (%)	10,488	53.6±10.8	24.0±8.3	<0.001
Use of ACEIs/ARBs	10,488	6600 (70.0)	989 (93.9)	<0.001
Use of statins	10,488	5790 (61.4)	840 (79.8)	<0.001
Use of β-blockers	10,488	6673 (70.7)	996 (94.6)	<0.001
Smoking status	10,488			0.72
No		7670 (81.3)	855 (81.2)	
Yes		591 (6.3)	72 (6.8)	
Missing		1174 (12.4)	126 (12.0)	
Insurance group	10,488			0.84
Private		1671 (17.7)	182 (17.3)	
Medicare/Medicaid		7545 (80.0)	844 (80.2)	
Missing		219 (2.3)	27 (2.6)	

Data are given as *n* (%) or means±SD unless otherwise indicated. ICD, implantable cardioverter-defibrillator; BMI: body mass index; LVEF, left ventricular ejection fraction; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

0.77) and 0.65 (95% CI, 0.50 to 0.85), respectively. No such association was noted among those with an eGFR<30 ml/min per 1.73 m^2 (Table 3).

Sensitivity Analyses

In the adjusted Cox proportional hazards model that included only patients who had ICDs placed after second eGFR<60 ml/min per 1.73 m^2 along with their corresponding controls (*n*=602), ICD was associated with lower mortality (HR, 0.73; 95% CI, 0.57 to 0.93). The interaction between ICD and eGFR stage did not reach significance (*P*=0.20), but the effect estimates were in the same direction as in the primary analysis (eGFR 45–59 ml/min per 1.73 m^2: HR, 0.54; 95% CI, 0.34 to 0.84; eGFR 30–44 ml/min per 1.73 m^2: HR, 0.70; 95% CI, 0.48 to 1.04; and eGFR<30 ml/min per 1.73 m^2: HR, 0.94; 95% CI, 0.61 to 1.45).

In another adjusted Cox proportional hazards model, we included patients who had an ICD before they developed CKD (two eGFR values <60 ml/min/per 1.73 m^2 90 days apart) and controls. In this subset (*n*=660), presence of an ICD was associated with lower mortality (HR, 0.66; 95% CI, 0.52 to 0.84; *P*<0.001). The interaction between ICD and eGFR stage did not reach significance (*P*=0.11), but the effect estimates were in the same direction as in the primary analysis (eGFR of 45–59 ml/min per 1.73 m^2: HR, 0.62; 95% CI, 0.43 to 0.91; eGFR of 30–44 ml/min per 1.73 m^2: HR, 0.62; 95% CI, 0.43 to 0.90; and eGFR<30 ml/min per 1.73 m^2: HR, 1.14; 95% CI, 0.68 to 1.91).

In the adjusted Cox proportional hazards model that included all patients with an ICD and all potential controls without matching (*n*=10,488 and *n*=3979 deaths, respectively), we also found a significant interaction between ICD and eGFR stage (*P*=0.01). Presence of an ICD was

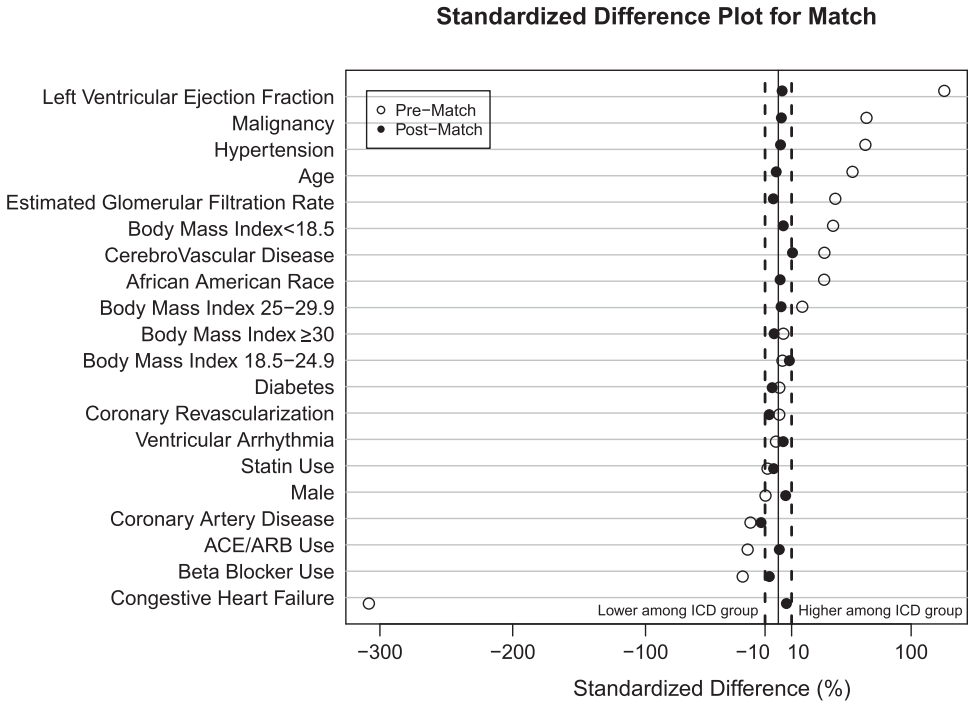

Figure 2. | **Standardized difference plot for match.** ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ICD, implantable cardioverter defibrillator.

associated with lower mortality among patients with an eGFR of 45–59 ml/min per 1.73 m^2 (HR, 0.68; 95% CI, 0.57 to 0.82) and an eGFR of 30–44 ml/min per 1.73 m^2 (HR, 0.65; 95% CI, 0.54 to 0.78), but no such association was noted among those with an eGFR<30 ml/min per 1.73 m^2 (HR, 1.0; 95% CI, 0.79 to 1.25). In a sensitivity analysis including only patients with no prior history of baseline malignancy (n=8059), similar results were noted (data not shown). In a sensitivity analysis by censoring at the time of transitioning to dialysis, similar results were seen (eGFR of 45–59 ml/min per 1.73 m^2: HR, 0.36; 95% CI, 0.24 to 0.52; eGFR of 30–44 ml/min per 1.73 m^2: HR, 0.55; 95% CI, 0.38 to 0.77; eGFR<30 ml/min per 1.73 m^2: HR, 0.85; 95% CI, 0.54 to 1.33).

Discussion

A significant proportion of patients with kidney disease die of cardiovascular disease before reaching dialysis (19). More importantly, sudden cardiac death contributes to a significant proportion of these deaths; thus, ICDs are postulated to confer survival advantage to this population. In this propensity-matched study of patients with CKD who had similar left ventricular and kidney function, we report that the presence of an ICD was associated with lower mortality in those with stage 3 CKD, but not among those with stage 4 CKD.

Patients with stages 1 and 2 CKD who receive an ICD tend to have similar survival advantage compared with those with preserved kidney function (20). On the other hand, patients with ESRD do not appear to have similar survival benefit when ICDs were implanted for primary prevention (21). However, only few studies examined the benefits of ICD placement in a nondialysis-dependent CKD population, and it seems that much of the decision-making regarding device therapy in this group is not based on clinical trial evidence. Among those with an ICD, a decrement in kidney function was associated with increased mortality (12%–16% increased mortality for each 10-ml/min per 1.73 m^2 lower eGFR) (14,22). More recently, Singh *et al.* reported that the presence of an ICD in those with stage 4 CKD (n=108) was not associated with lower mortality (23). Another study examining the National Cardiovascular Data Registry ICD registry reported that the risk of death after primary prevention ICD placement is proportional to CKD severity (24). However, the lack of a control group of patients with CKD without an ICD precludes us from excluding the potential benefits of ICDs in this population. In a patient-level meta-analysis of seven clinical trials, Pun *et al.* showed that the differences in baseline eGFR decrease the survival benefits of those receiving an ICD (25). However, very few patients with an eGFR<30 ml/min per 1.73 m^2 were included in this analysis, arguing for additional studies.

In our study, survival benefit was noted in those with stage 3 CKD, a category that constitutes the vast majority of nondialysis-dependent CKD. Kidney disease increases the risk of arrhythmic complications to an extent that cannot be explained by the severity of the atherosclerotic process (26,27). Several underlying pathophysiologic processes, including electrolyte imbalance, autonomic disturbances, and uremic cardiomyopathy, may explain the higher risk of sudden cardiac death (26). Although the magnitude of benefit might be lower with decline in kidney function, the observed protective associations by us and others suggest the utility of transvenous ICDs in this large segment of the nondialysis-dependent CKD population (25,28).

Table 2. Patient characteristics by presence of ICD after propensity match

Factor	Non-ICD Group (*n*=631)	ICD Group (*n*=631)	*P* Value
Age	72.0±10.8	70.5±11.6	0.02
Men	439 (69.6)	428 (67.8)	0.50
Black race	128 (20.3)	111 (17.6)	0.22
BMI (kg/m^2)	28.4±6.1	28.9±6.0	0.19
BMI group (kg/m^2)			0.65
<18.5	6 (0.95)	4 (0.63)	
18.5–24.9	182 (28.8)	173 (27.4)	
25–29.9	233 (36.9)	219 (34.7)	
≥30	206 (32.6)	231 (36.6)	
Missing	4 (0.63)	4 (0.63)	
eGFR (ml/min per 1.73 m^2)	42.2±11.8	42.8±11.6	0.33
CKD stage, by eGFR (ml/min per 1.73 m^2)			0.11
45–59	305 (48.3)	303 (48.0)	
30–44	219 (34.7)	227 (36.0)	
15–29	91 (14.4)	96 (15.2)	
<15	16 (2.5)	5 (0.79)	
Diabetes	186 (29.5)	192 (30.4)	0.71
Hypertension	486 (77.0)	488 (77.3)	0.89
Congestive heart failure	338 (53.6)	347 (55.0)	0.61
Coronary artery disease	338 (53.6)	333 (52.8)	0.78
Cerebrovascular disease	82 (13.0)	90 (14.3)	0.51
Peripheral vascular disease	33 (5.2)	31 (4.9)	0.80
Coronary revascularization	88 (13.9)	91 (14.4)	0.81
Ventricular arrhythmia	18 (2.9)	31 (4.9)	0.06
Albumin (g/dl)	4.0±0.50	4.0±0.50	0.04
Hemoglobin (g/dl)	12.3±1.9	12.5±1.9	0.02
LVEF (%)	26.7±9.2	27.2±8.2	0.28
Malignancy	115 (18.2)	99 (15.7)	0.23
Use of ACEIs/ARBs	573 (90.8)	576 (91.3)	0.77
Use of statins	480 (76.1)	490 (77.7)	0.50
Use of β-blockers	577 (91.4)	581 (92.1)	0.68
Smoking			0.42
No	488 (77.3)	506 (80.2)	
Yes	51 (8.1)	48 (7.6)	
Missing	92 (14.6)	77 (12.2)	
Insurance			0.15
Private	129 (20.4)	107 (17.0)	
Medicare/Medicaid	481 (76.2)	509 (80.7)	
Missing	21 (3.3)	15 (2.4)	

Data are given as *n* (%) or means±SD unless otherwise indicated. ICD, implantable cardioverter-defibrillator; BMI: body mass index; LVEF, left ventricular ejection fraction; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

However, we did not observe a similar protective association of ICDs among the stage 4 CKD population. A recent pooled analysis of clinical trials that examined the benefits of ICDs noted that the presence of higher comorbidities (four versus two) was associated with higher mortality rates in those with an ICD (16). This report argued for real-world outcomes data of medically complex patients receiving ICDs. Patients with CKD (particularly with advanced kidney disease) sustain higher comorbidity burden, and as such could explain the lack of association noted in those with stage 4 CKD. We matched the ICD group based on several different comorbidities, including cardiac and kidney function, and had a reasonable number of patients with stage 4 CKD. The preponderance of non-arrhythmic deaths in those with advanced kidney disease (stage 4 CKD) and heart failure might explain the lack of association in stage 4 CKD. Deaths in our cohort were not adjudicated for arrhythmic versus other causes of death and future studies should examine such differences.

Apart from higher costs, other issues merit consideration when deciding about ICD implantation in patients with kidney disease. Procedure-related complications, particularly hematoma at the site of ICD implantation, are higher in those with kidney disease than those without (29). We recently noted that ICD-related infections among dialysis patients were associated with higher length of stay and mortality (30). Although it is unknown whether this higher risk is present in individuals with nondialysis-dependent CKD, recent studies have shown higher risk for infections in this population and this should be also be taken into consideration before ICD placement in these patients (31).

Strengths of this analysis include the large sample size (both for stage 3 and stage 4 CKD), the diverse patient population, and the availability of comprehensive data, including

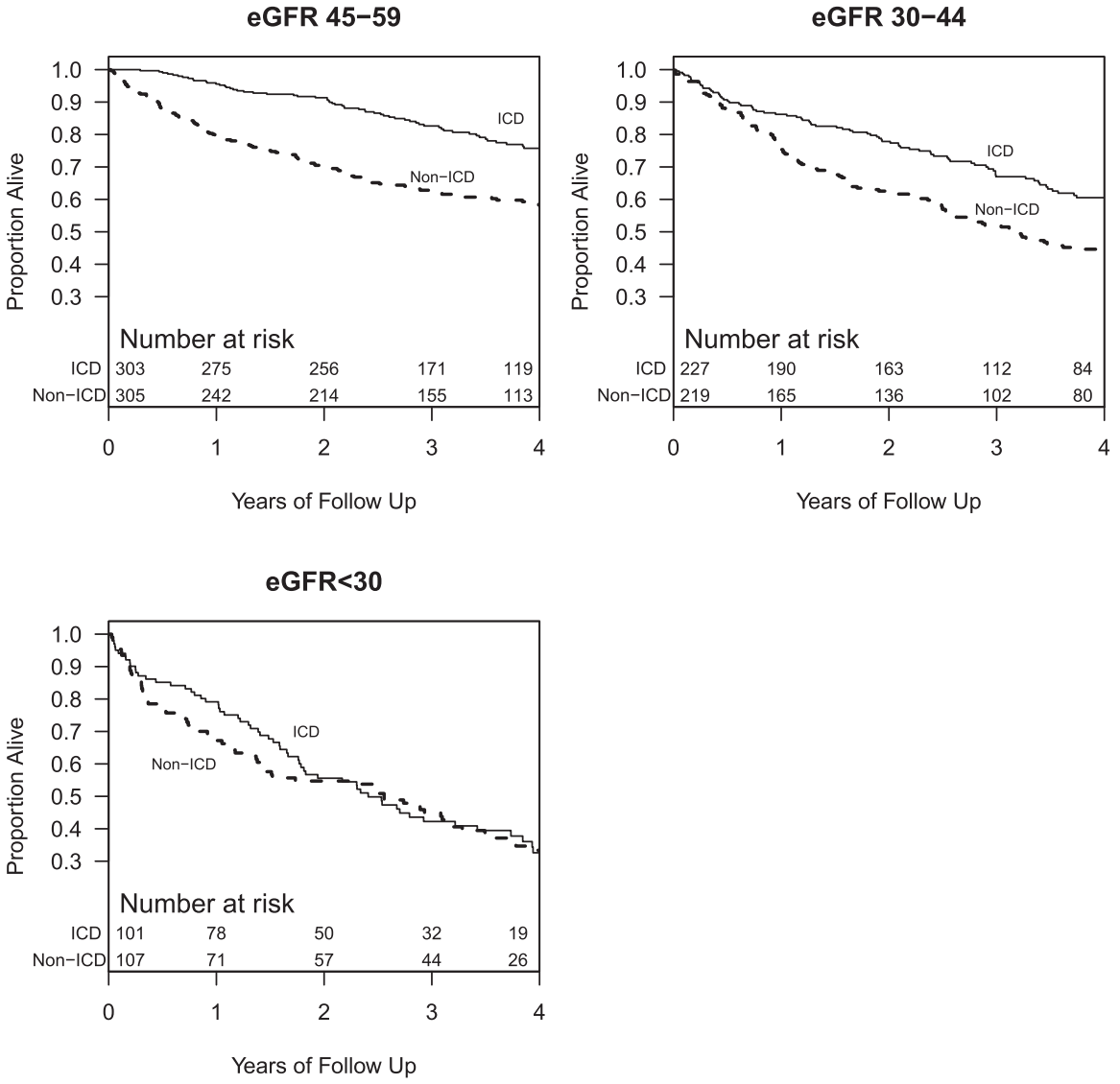

Figure 3. | Kaplan–Meier curves showing survival of those with and without an implantable cardioverter defibrillator for various eGFR categories. ICD, implantable cardioverter defibrillator.

the cardiovascular and kidney function data for the study cohort. Previous studies lacked details related to patients who progressed to dialysis, and our sensitivity analysis findings further confirm the protective associations of ICDs in those with stage 3 CKD. We attempted to avoid the inherent bias of an observational study by using a propensity matched cohort, and the c-statistic of the logistic model for the propensity score was 0.97, suggesting the reliability of the model. However, our

Table 3. Associations of ICD with death among propensity-matched patients

Association	Unadjusted Model	Adjusted Model[a]
ICD (versus no ICD)—overall	0.65 (0.55 to 0.77)	0.69 (0.59 to 0.82)
ICD interaction with eGFR stage (ml/min per 1.73 m^2)		
45–59	0.55 (0.42 to 0.73)	0.58 (0.44 to 0.77)
30–44	0.64 (0.49 to 0.83)	0.65 (0.50 to 0.85)
<30	0.92 (0.67 to 1.27)	0.98 (0.71 to 1.35)

Data are presented as hazard ratios (95% confidence intervals). ICD, implantable cardioverter-defibrillator.
[a]Adjusted for age, ventricular arrhythmia, hemoglobin, albumin, and indicators for missing values.

study is subject to other limitations, including the fact that the data are primarily from a single major health care system. The decision to place an ICD is often complex, and residual confounding might still be present despite the propensity matching. Furthermore, we lacked details about prior history of myocardial infarction, hospitalization details for heart failure and other reasons, and admissions to a nursing home or skilled nursing facility. Higher urinary protein excretion is associated with higher cardiovascular mortality. We did not have details about proteinuria for all of the study participants; hence, this was not included in the propensity matching. We were only able to match 62% of patients who received an ICD. There were still differences between groups on some variables (*e.g.*, age and ventricular arrhythmia), which we adjusted for in the final Cox proportional hazards model. In addition, we conducted a Cox proportional hazards model that included all patients, which yielded similar results. The control group had similar left ventricular ejection fraction and comorbid conditions but did not receive ICDs, which suggests that this group could be sicker or this treatment difference could be related to provider bias. However, we included several key medical problems, including patient nutritional status details, in the analysis to account for this. We also lacked cause-of-death details to determine whether the survival benefit relates to improvements in arrhythmic deaths, which could be a topic of future investigations.

In summary, in a large cohort matched for demographics, comorbidities, and cardiac and kidney function, presence of an ICD was associated with lower mortality in those with stage 3 CKD, but not in those with stage 4 CKD. Although cumulative evidence supports the benefits of ICDs in stage 3 CKD, further clinical trials examining the benefits and other complications of ICDs in this population are warranted to support ICD placement in the stage 4 CKD population.

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Disclosures

B.L.W. served on the Physician Advisory Boards for Medtronic, St. Jude Medical, Boston Scientific, and Spectranetics.

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