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Kidney function and appropriateness of device therapies in adults with implantable cardioverter defibrillators

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Abstract

Objective—Patients with chronic kidney disease (CKD) have higher risk of sudden cardiac death; however, they may not receive implantable cardioverter defibrillators (ICDs), in part due to higher risk of complications. We evaluated whether CKD is associated with greater risk of device-

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delivered shocks/antitachycardia pacing (ATP) therapies among patients receiving a primary prevention ICD.

Methods—We studied participants in the observational Cardiovascular Research Network Longitudinal Study of Implantable Cardioverter Defibrillators. CKD was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². Outcomes included all delivered shocks/ATPs therapies and type of shock/ATP therapies (inappropriate or appropriate, determined by physician adjudication) within the 3 years. We evaluated the associations between CKD and time to first device therapy, burden of device therapy, and inappropriate versus appropriate device therapy, adjusting for demographics, comorbidity, laboratory values and medication use.

Results—Among 2161 participants, 1066 (49.3%) had CKD (eGFR 44 ± 11 mL/min/1.73 m²) at ICD implantation. During mean of 2.26 ± 0.89 years, 9.8% and 18.5% of participants had at least one inappropriate and appropriate shock/ATP therapies, respectively. CKD was not associated with time to first shock/ATP therapies (adjusted HR 0.87, 95% CI 0.73 to 1.05), overall burden of shock/ATP therapies (adjusted relative rate 0.93, 95% CI 0.74 to 1.17) or inappropriate versus appropriate shock/ATP therapies (adjusted relative risk 0.88, 95% CI 0.68 to 1.14) compared with not having CKD.

Conclusions—In adults receiving a primary prevention ICD, mild-to-moderate CKD was not associated with the timing, burden or appropriateness of subsequent device therapy. Potential concern for inappropriate ICD-delivered therapies should not preclude ICDs among eligible patients with CKD.

INTRODUCTION

Chronic kidney disease (CKD) affects ~14% of adults in the USA.¹ Sudden cardiac death (SCD) is more frequent in patients with CKD and remains one of the primary causes of death among these vulnerable patients. Even small decreases in kidney function are associated with increased risk of SCD.² Patients with CKD have many factors that make them vulnerable for SCD including more frequent and severe left ventricular hypertrophy,³ enhanced myocardial ischaemia and fibrosis⁴ and vascular stiffness.⁵ Patients with CKD also have several possible proarrhythmogenic triggers as a consequence of their kidney dysfunction, including electrolyte abnormalities, greater inflammation,⁶ sympathetic nervous system dysregulation⁷ and cardiovascular stress induced by volume overload.⁸

Implantable cardioverter defibrillators (ICDs) as a primary prevention strategy for SCD have been proven to reduce the risk of death in adults with heart failure (HF) and reduced left ventricular ejection fraction (LVEF) when compared against optimal medical therapy alone.^{9,10} Despite being at higher risk for cardiovascular events, patients with CKD are often less likely to receive medically indicated cardiovascular therapies and procedures compared with patients who do not have CKD, which has been termed ‘renalism’.¹¹ While specific reasons for this are not always clear, observational studies have shown that in patients with end-stage renal disease, ICDs for primary prevention of SCD are associated with a higher risk of adverse device-related outcomes compared with patients without kidney disease.¹² Patients with CKD may be at higher risk for inappropriate shock or antitachycardia pacing (ATP) therapy as well due to renal-related metabolic derangements (eg, hyperkalemia¹³) and

the high prevalence of supraventricular arrhythmias (eg, atrial fibrillation)¹⁴ in this population. Inappropriate shocks are associated with subsequently poorer quality of life, higher risk of death and higher medical costs.¹⁵¹⁶

However, there is a paucity of literature that has quantified this risk of appropriate and/or inappropriate shocks/ATPs therapies among patients with CKD who undergo primary prevention ICD implantation compared with those who have preserved kidney function. Existing studies have been limited by small sample sizes and possible ascertainment bias, which may have limited characterisation of ‘appropriateness’ of delivered shocks.^{17–20} To address this knowledge gap, we used the Cardiovascular Research Network Longitudinal Study of Implantable Cardioverter Defibrillator (CVRN LS-ICD) cohort²¹—a multicentre well-characterised cohort of patients with HF and reduced LVEF who underwent a primary prevention ICD implant and who had rigorous adjudication of subsequently delivered ICD therapies—to examine the association of CKD with occurrence and types of device therapies (inappropriate or appropriate shocks/ATPs therapies). We hypothesised that patients with CKD would have higher rates of both appropriate and inappropriate shocks compared with those without CKD.

METHODS

Study population

The study population included patients from the CVRN LS-ICD cohort, which consists of 2787 adult members from seven participating healthcare systems (Kaiser Permanente Northern California, Kaiser Permanente Colorado, Kaiser Permanente Northwest, Kaiser Permanente Southern California, Fallon Community Health Plan, Marshfield Clinic Research Foundation in Wisconsin and Henry Ford Health System in Michigan), with left ventricular systolic dysfunction who received a first-time ICD between 1 January 2006 and 31 December 2009 for primary prevention of SCD.²¹ The CVRN LS-ICD cohort linked data from three sources: the American College of Cardiology National Cardiovascular Data Registry (NCDR) ICD Registry for baseline indicators, individual health system data and an adjudicated repository of treated arrhythmic episodes.

We excluded CVRN LS-ICD participants who had less than 1 year of continuous membership before their initial ICD implantation (n=547) to ensure more complete data on patient characteristics; who were less than 21 years old (n=3); who died during the index admission (n=7); who were missing serum creatine measurement (n=12); who were receiving dialysis at the time of ICD implantation (n=75) or who had a history of kidney transplant at the time of ICD placement (n=15). We chose to exclude patients on dialysis as this group is distinctly different from those with non-dialysis requiring CKD and given the potential influence of the dialysis therapy itself rather than underlying native level of kidney function. We also excluded participants with LVEF < 35% (n=293) and those with a history of monomorphic ventricular tachycardia (n=41) since these patients did not meet criteria for primary prevention ICD. Application of these exclusion criteria yielded a final analytic sample of 1916 participants.

The study was approved by the appropriate institutional review board committees at each site. Waiver of informed consent was obtained due to the nature of the study.

Primary exposure

The main exposure was level of kidney function at the time of ICD implantation. We used serum creatine concentration values found in the NCDR ICD Registry at the time of ICD placement to calculate preimplantation estimated glomerular filtration rate (eGFR) using the recommended CKD-EPI estimating equation.²² The CKD-EPI equation was developed to create a more precise formula to estimate GFR from serum creatine and other clinical parameters (age, sex, race). The equation was developed using 10 studies and externally validated in a dataset of 16 studies. The CKD-EPI equation performed better than the Modification of Diet and Renal Disease Study equation, especially at higher GFR, with less bias and greater accuracy.²² We initially classified patients into National Kidney Foundation-recommended categories of eGFR (mL/min/1.73 m²): ≥60, 45–59, 30–44, 15–29 and <15 not receiving dialysis.²³ However, given the small number of participants with very low eGFR, in main analyses we focused on the following comparisons: eGFR <60 vs ≥60 and <45 vs ≥45 mL/min/1.73 m².²³

Outcomes

Patients were followed for a maximum of 3 years after receiving the ICD implant or until 31 December 2011. Range of follow-up was 0.2 months to 3.04 years. We censored patients at the time of death, health plan disenrollment, receipt of 10 device therapies or end of follow-up.

The main outcomes included documented receipt of a device-delivered therapy (shock or ATP therapies), overall and by type (appropriate, inappropriate or unable to determine). The rigorous adjudication process included manual medical record abstraction at the study sites with central clinical review and external expert adjudication of source documentation as described previously.²¹ A central physician review panel (blinded to participants' level of kidney function) (1) confirmed or refuted the occurrence of treated episodes, (2) determined the initial type of therapy (ATP therapies or shock), (3) determined whether the episode required multiple therapies and (4) adjudicated the appropriateness of therapy using standardised criteria. Records were further reviewed by an external panel of three expert electrophysiologists. Each record was reviewed independently by two of the four central panellists, with resolution of any discrepancies through arbitration by the external expert panel as needed.

Covariates

We ascertained baseline information from data collected by the NCDR ICD Registry,²⁴ as well as from health plan electronic medical records during a 3 year period prior to ICD placement, based on relevant *International Classification of Diseases, Ninth Edition* diagnosis and procedure codes, laboratory test results and medications.^{21,25} We collected data on age at the time of ICD placement, gender, self-reported race and ethnicity, tobacco use, New York Heart Association class, known ischaemic heart disease, previous myocardial infarction, previous coronary artery bypass surgery, previous percutaneous coronary

intervention, atrial fibrillation or flutter, previous valvular surgery, cerebrovascular disease, diabetes mellitus, hypertension, dyslipidemia, lung disease and liver disease. We also included the most recent ambulatory systolic blood pressure, body mass index, type of ICD device implanted and LVEF prior to ICD placement. We further collected information on receipt of ACE inhibitors (ACEi)/angiotensin II receptor blockers (ARBs), β -blockers and diuretics at discharge following device implant.

Analytic approach

Analyses were conducted using SAS, V.9.3. We compared baseline characteristics across eGFR categories (≥ 60 vs <60 mL/min/1.73 m²) using analysis of variance for continuous variables and χ^2 tests for categorical variables.

Our main goal was to examine the associations between eGFR and three aspects of device therapy: (1) time to first device therapy, overall and separately by type of therapy (inappropriate and appropriate), (2) burden of all device therapies, overall and separately by type of therapy, and (3) proportion of inappropriate versus appropriate device therapies. We first determined the number of patients who received shocks/ATPs therapies, the total number of shocks/ATPs therapies received as well as appropriate versus inappropriate shock/ATP therapy. For each outcome, we performed serial regression models that first started with an unadjusted model, followed by sequential addition of demographic data, baseline medical history and laboratory results, and baseline medication use. Robust SE estimates were used in all analyses.

We used Cox proportional hazards regression to quantify the association between eGFR and time to first shock/ATP therapies (any, inappropriate, appropriate). We confirmed that the proportional hazards assumption was not violated by visual inspection of log-negative-log survival curves. We used Poisson regression to quantify the association between eGFR and counts of shock/ATP therapies (any, inappropriate, appropriate) during the follow-up period. Finally, we used relative risk regression to quantify the association between eGFR and appropriateness of device therapy. Relative risk estimates for the binary outcome (inappropriate vs appropriate shock/ATP therapies) were calculated using Poisson regression software with robust SEs.²⁶

In a sensitivity analysis, we used the Fine and Gray method to perform a competing risk analysis accounting for risk of all-cause mortality in our models testing the association of eGFR with time to first shock/ATP therapies.

RESULTS

Among 1916 eligible participants, 949 (49.5%) had CKD at the time of primary prevention ICD implantation. The mean $\pm$ SD eGFR for those with CKD was 44 ± 11 mL/min/1.73 m² measured at a median time of 1 (IQR 0–8) day prior to ICD implantation. Those with CKD were more likely to be older and have greater comorbidity (table 1).

Among the study population, a total of 1717 confirmed shocks/ATP therapies were identified and 26.9% of participants had at least one shock/ATP therapies during a mean

follow-up time of 2.26 ± 0.89 years. In the study population, 18.3% had at least one appropriate shock/ATP therapies and 9.8% had at least one inappropriate shock/ATP therapies. The proportion of participants who had at least one shock/ATP therapies decreased with declining eGFR categories (table 2). Similarly, the proportion of participants with at least one inappropriate shock/ATP therapies or appropriate shock/ATP therapies was decreased with lower eGFR (table 2). Among those who received a shock/ATP therapies during follow-up, the median (IQR) number of delivered shocks/ATPs therapies overall was 2.0 (1.0–5.0) and was similar across eGFR categories except for the lowest categories where more shocks/ATPs therapies were delivered.

For the outcome of *time to first shock/ATP therapy*, participants with eGFR <60 mL/min/ 1.73 m² had a 19% lower relative hazard of a shock/ATP therapies compared with participants with eGFR ≥ 60 mL/min/ 1.73 m² in unadjusted models. After multivariable adjustment, this association was no longer statistically significant (figure 1A). In unadjusted models, participants with eGFR <60 mL/min/ 1.73 m² had 30% lower relative hazard of an inappropriate shock/ATP therapies compared with those who had eGFR ≥ 60 mL/min/ 1.73 m², but this association was not significant after adjustment for demographics and clinical site (figure 1A). There was no association between lower eGFR with risk of appropriate shock/ATP therapies in unadjusted or multivariable models (figure 1A). Similar findings were noted when participants with eGFR <45 mL/min/ 1.73 m² were compared with those with eGFR ≥ 45 mL/min/ 1.73 m² (figure 1B). In a sensitivity analysis, we performed models to account for competing risk of all-cause mortality. Results were consistent with the primary analysis (see online supplementary table S1).

For the outcome of *burden of device therapy*, participants with eGFR <60 mL/min/ 1.73 m² were not at greater risk for more shocks/ATPs therapies compared with those with eGFR ≥ 60 mL/min/ 1.73 m² in unadjusted or adjusted models (figure 2A). Similar results were observed for burden of inappropriate or appropriate device therapies in those with eGFR <60 vs ≥ 60 mL/min/ 1.73 m² (figure 2A). In addition, results were similar when comparing eGFR <45 vs ≥ 45 mL/min/ 1.73 m² (figure 2B).

Finally, in evaluating *appropriateness of device therapy*, there was no significant association between eGFR <60 mL/min/ 1.73 m² and receiving inappropriate versus appropriate shock/ATP therapy compared with eGFR ≥ 60 mL/min/ 1.73 m² (figure 3A). Similar results were observed when comparing eGFR <45 vs ≥ 45 mL/min/ 1.73 m² (figure 3B).

DISCUSSION

In this large ‘real-world’ cohort of patients who underwent primary prevention ICD placement, we found little evidence that rates of shock and ATP therapy were different among those with and without CKD. Furthermore, despite having a worse clinical profile, patients with CKD were not more likely to receive inappropriate shocks compared with those without CKD. These data suggest that potential concerns for more frequent or inappropriate ICD therapies should not preclude appropriate primary prevention ICD implantation among patients with CKD, who are known to be at high risk for SCD.

Our finding that patients with CKD had similar rates of appropriate shocks/ATPs therapies after primary prevention ICD implantation compared with patients without CKD differs from other studies that reported *higher* risks of appropriate shocks among patients with $\text{eGFR} < 60 \text{ mL/min/1.73 m}^2$.^{17,18} One single-centre study of 509 patients reported that those with advanced stages of CKD (defined as $\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$) had a more than twofold higher risk of appropriate shocks after ICD implantation.¹⁷ When we examined patients with more advanced CKD ($\text{eGFR} < 45 \text{ mL/min/1.73 m}^2$) in our study, we did not find a statistically significant association of advanced CKD with higher risk of appropriate shocks. We had relatively few patients with $\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$, so were not able to examine this group separately. However, our study's findings among a much larger and more generalisable multi-institutional cohort support and extend those reported by other investigators. A recent analysis found no association between kidney function and risk of appropriate delivered ICD therapies.²⁰ There are several notable limitations in these prior reports that our study improves on; for example, in prior studies, ATPs therapies were not captured, the determination of 'appropriateness' was not determined by rigorous adjudication processes and sample size was limited and/or from a single centre. Another key difference between our study population and others was the rate of concomitant cardiovascular medication use, which was quite high compared with previous studies. For example, ~50% of patients in the previous study were reportedly taking β -blockers compared with >90% in our study. Our findings raise the possibility that with optimal medical treatment of HF and cardiovascular disease, patients with CKD may not be at greater risk of malignant ventricular arrhythmias compared with those who did not have CKD.

Our finding that patients with CKD were *not* at higher risk of inappropriate shock/ATP therapies is contrary to common perceptions among providers. In the Multi-center Automatic Defibrillator Implantation Trial II (MADIT II trial), ~11.5% of patients experienced an inappropriate shock (similar to the estimates in our study population).¹⁵ The most common triggers for inappropriate shock were atrial fibrillation and other supraventricular tachycardias. Patients with CKD are plausibly at higher risk for inappropriate shocks due to higher burden of metabolic derangements (eg, hyperkalemia) and supraventricular arrhythmias. The patients with CKD in our study had potassium values within the high normal range (with the majority being on ACEi or ARBs) and 35% had atrial fibrillation at the time of ICD implantation. Despite these possible triggers, the rates of inappropriate shocks were similar in those with versus without CKD. Receipt of inappropriate ICD therapies has serious consequences such as higher risk of death,¹⁶ higher healthcare costs and poorer quality of life.²⁷ Our findings in a large, multicentre population with adjudicated device therapies suggest that risk of inappropriate shocks should not preclude primary prevention ICD implantation in patients with CKD, although future trials would also help inform this question.

Numerous studies have focused on long-term clinical outcomes such as death among patients with CKD who receive a primary prevention ICD. For example, in a post hoc analysis of the MADIT-II and SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) randomised trials, there was a 51% lower adjusted rate of death after primary prevention ICD placement in patients with $\text{eGFR} \geq 60 \text{ mL/min/1.73 m}^2$, but no survival benefit in

patients with CKD.²⁸²⁹ Among Medicare beneficiaries, CKD was associated with a 2.3-fold higher rate of death after ICD implantation.³⁰ While these findings are important, it remains unclear what is contributing to these poor outcomes among patients with CKD. Our findings suggest that differential rates of delivered ICD shocks/ATPs therapies as well as type of shock/ATP therapies (inappropriate and appropriate) do not explain the increased risk of death in patients with CKD with a primary prevention ICD.

Our study has important clinical implications. Patients with CKD are often victim to 'renalism',¹¹ particularly regarding cardiovascular procedures and therapies. With the growing population of patients with both CKD and HF, more patients will be facing the decision about primary prevention ICD implantation. Therefore, it is important to have a comprehensive understanding of the associated risks and benefits of ICD implantation in the setting of CKD, including short-term outcomes that may directly affect a patient's quality of life. Our study is a first step in quantifying risks of ICD-related adverse outcomes in CKD. Recognising that decisions around ICD implantation are complex and multifaceted, further work with both observational studies and clinical trials is needed to better quantify the overall short-term and long-term risks and benefits with ICD implantation in patients with CKD.

There were several strengths of our study. We studied a large, multicentre patient population with systolic HF treated in usual care, with available serum creatine measures proximal to ICD implantation. Our outcomes related to device therapies were ascertained through rigorous abstraction and clinical expert adjudication. We were able to adjust for a number of important covariates including cardiovascular medication use. We recognise a few limitations as well. CKD status was defined by a single measure of serum creatine at the time of ICD implantation. We had relatively few patients with advanced stages of CKD (including chronic dialysis), which precluded rigorous evaluation in this subgroup. However, patients with mild-to-moderate stages of CKD comprise a substantial proportion of patients with HF. By nature of the design of the LS-ICD study, patients were followed up to 3 years after ICD implantation. The settings for the ICD device were not systematically available for this analysis. Finally, patients in the study were enrolled in healthcare delivery systems and thus may not be completely generalisable to uninsured patient populations.

In conclusion, among a large, multicentre, well-treated cohort of patients with HF and reduced LVEF who underwent primary prevention ICD implantation, we found that level of mild-to-moderate CKD was not significantly associated with risks of device therapy, burden of device therapy and appropriateness of delivered shocks/ATPs therapies. This study provides data on important short-term outcomes that are often considered by both the patient and provider in decision making around ICD implantation. Clinical trials are needed to evaluate the overall short-term and long-term risks and benefits of primary prevention ICDs in the high-risk and growing patient population of patients with CKD with HF.

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Key messages

What is already known on this subject?

Patients with chronic kidney disease (CKD) are at higher risk for sudden cardiac death and may benefit from implantable cardioverter defibrillator (ICD) implantation. However, patients with CKD may be at higher risk for complications, such as inappropriate shocks from metabolic derangements or other triggers.

What might this study add?

This study examines the association of kidney function with risk of appropriate and inappropriate antitachycardia pacing (ATPs)/shocks among patients with a primary prevention ICD. We found that CKD was not associated with time to first shock/ATP therapies (adjusted HR 0.87, 95% CI 0.73 to 1.05), overall burden of shock/ATP therapies (adjusted relative rate 0.93, 95% CI 0.74 to 1.17) or inappropriate versus appropriate shock/ATP therapies (adjusted relative risk 0.88, 95% CI 0.68 to 1.14) compared with not having CKD.

How might this impact on clinical practice?

Given our findings, concern for greater risk of inappropriate shocks/ATPs therapies should not preclude ICD implantation among patients with CKD who are otherwise eligible for ICD. This is important for practicing cardiologists, nephrologists and internists who frequently see these patients and make decision regarding cardiovascular devices.

Figure 1.

Association (HR with 95% CI) of baseline estimated glomerular filtration rate (eGFR) and risk of any delivered shock/antitachycardia pacing among participants with a primary prevention implantable cardioverter defibrillator comparing (a) those with eGFR <60 vs ≥ 60 mL/min/1.73 m² and (b) those with eGFR <45 vs ≥ 45 mL/min/1.73 m² (n=2161).

Figure 2.

Association (relative risk with 95% CI) of baseline estimated glomerular filtration rate (eGFR) and burden of total delivered shocks/antitachycardia pacing therapies among participants with a primary prevention implantable cardioverter defibrillator comparing (a) those with eGFR <60 vs ≥60 mL/min/1.73 m² and (b) those with eGFR <45 vs ≥45 mL/min/1.73 m² (n=2161).

Figure 3.

Association (relative risk with 95% CI) of baseline estimated glomerular filtration rate (eGFR) with risk of receiving an inappropriate shock/anti-tachycardia pacing (ATP) versus appropriate shock/ATP therapies among participants with a primary prevention implantable cardioverter defibrillator (ICD) who received a device therapy comparing (a) those with eGFR <60 vs ≥60 mL/min/1.73 m² and (b) those with eGFR <45 vs ≥45 mL/min/1.73 m² (n=1812). Model 1: age, gender, race and site. Model 2: model 1 + New York Heart Association class, ischaemic heart disease, hypertension, dyslipidemia, previous myocardial infarction, previous coronary artery bypass surgery, previous percutaneous coronary intervention, atrial fibrillation or flutter, ventricular tachycardia, previous valvular surgery, tobacco use, cerebrovascular disease, diabetes, lung disease, liver disease, systolic blood pressure, body mass index and left ventricular ejection fraction. Model 3: model 2 + ICD device type, ACE inhibitors/angiotensin II receptor blockers, β -blockers and diuretics.

Table 1

Baseline characteristics of adults receiving ICD

Characteristic	Overall (n=1916)	eGFR 60 mL/min/ 1.73 m ² (n=967)	eGFR <60 mL/min/ 1.73 m ² (n=949)	p Value
Age (years), mean (SD)	68.3 (11.1)	64.5 (11.8)	72.1 (8.9)	<0.001
Women, n (%)	497 (25.9)	220 (22.8)	277 (29.2)	<0.001
Race, n (%)				0.19
White/European	1469 (76.7)	751 (77.7)	718 (75.7)	
Black/African-American	289 (15.1)	151 (15.6)	138 (14.5)	
Current or former tobacco use, n (%)	827 (43.2)	430 (44.5)	397 (41.8)	0.25
ICD device type				<0.001
Single chamber	631 (32.9)	372 (38.5)	259 (27.3)	
Dual chamber	651 (34.0)	324 (33.5)	327 (34.5)	
Biventricular	634 (33.1)	271 (28.0)	363 (38.3)	
Distribution of preimplantation left ventricular ejection fraction (%), mean (SD)	23.8 (5.7)	23.9 (5.8)	23.8 (5.6)	0.83
<i>Cardiac-related comorbidities, n (%)</i>				
Chronic heart failure duration *				0.02
Within 3 months	169 (8.8)	81 (8.4)	88 (9.3)	
3–9 months	213 (11.1)	120 (12.4)	93 (9.8)	
>9 months	1342 (70.0)	653 (67.5)	689 (72.6)	
Prior chronic heart failure hospitalisation *				0.005
None	800 (41.8)	418 (43.2)	382 (40.3)	
Within 6 months	488 (25.5)	222 (23.0)	266 (28.0)	
>6 months	420 (21.9)	204 (21.1)	216 (22.8)	
NYHA heart failure class *				<0.001
I	210 (11.0)	113 (11.7)	97 (10.2)	
II	954 (49.8)	529 (54.7)	425 (44.8)	
III	714 (37.3)	312 (32.3)	402 (42.4)	
IV	33 (1.7)	10 (1.0)	23 (2.4)	
Ischaemic heart disease	1199 (62.6)	534 (55.2)	665 (70.1)	<0.001
Previous myocardial infarction	969 (50.6)	432 (44.7)	537 (56.6)	<0.001
Previous coronary artery bypass surgery	580 (30.3)	234 (24.2)	346 (36.5)	<0.001
Atrial fibrillation or flutter	601 (31.4)	278 (28.7)	323 (34.0)	0.01
Hypertension	1401 (73.1)	661 (68.4)	740 (78.0)	<0.001
Dyslipidemia	1582 (82.6)	761 (78.7)	821 (86.5)	<0.001
Previous valvular surgery	108 (5.6)	53 (5.5)	55 (5.8)	0.77
Permanent pacemaker	171 (8.9)	67 (6.9)	104 (11.0)	0.002
Missing	3 (0.2)	1 (0.1)	2 (0.2)	
Cerebrovascular disease	270 (14.1)	109 (11.3)	161 (17.0)	<0.001
Chronic lung disease	378 (19.7)	183 (18.9)	195 (20.5)	0.37
Chronic liver disease	60 (3.1)	38 (3.9)	22 (2.3)	0.04

Characteristic	Overall (n=1916)	eGFR 60 mL/min/ 1.73 m ² (n=967)	eGFR <60 mL/min/ 1.73 m ² (n=949)	p Value
Diabetes mellitus	795 (41.5)	359 (37.1)	436 (45.9)	<0.001
Systolic blood pressure (mm Hg), mean (SD) *	124.0 (19.7)	123.6 (19.1)	124.3 (20.4)	0.46
Body mass index, mean (SD) *	28.7 (6.5)	29.5 (6.8)	27.8 (6.0)	<0.001
Serum creatine (μmol/L), mean (SD)	114.9 (79.6)	88.4 (17.7)	150.3 (106.1)	<0.001
Time of serum creatine from ICD implant, median (IQR)	-1.0 (-8.0 to 1.0)	-2.0 (-8.0 to 1.0)	-1.0 (-7.0 to 1.0)	0.02
Estimated glomerular filtration rate (mL/min/1.73 m ²), mean (SD)	61.1 (21.2)	78.2 (13.2)	43.7 (11.2)	<0.001
Sodium (mmol/L), mean (SD)	138.9 (3.4)	138.7 (3.8)	139.2 (3.0)	<0.001
Potassium (mmol/L), mean (SD) (available in 85.7% of patients) *	4.4 (0.5)	4.4 (0.4)	4.4 (0.5)	0.40
Haemoglobin (g/dL), mean (SD) (available in 84.5% of patients) *	13.6 (1.7)	13.9 (1.6)	13.2 (1.7)	<0.001
QRS duration, mean (SD) *	131.2 (34.6)	127.0 (33.8)	135.5 (34.9)	<0.001
ACE inhibitors	1314 (68.6)	711 (73.5)	603 (63.5)	<0.001
Angiotensin II receptor blockers	417 (21.8)	195 (20.2)	222 (23.4)	0.09
β-blocker	1742 (90.9)	886 (91.6)	856 (90.2)	0.28
Calcium channel blocker	118 (6.2)	54 (5.6)	64 (6.7)	0.29
Diuretic	1479 (77.2)	714 (73.8)	765 (80.6)	<0.001
Nitrate	572 (29.9)	236 (24.4)	336 (35.4)	<0.001
Antiarrhythmic agent	150 (7.8)	62 (6.4)	88 (9.3)	0.02
Digoxin	606 (31.6)	313 (32.4)	293 (30.9)	0.48
Statin	1481 (77.3)	712 (73.6)	769 (81.0)	<0.001
Aspirin	1243 (64.9)	626 (64.7)	617 (65.0)	0.90
Platelet aggregation inhibitor	268 (14.0)	128 (13.2)	140 (14.8)	0.34
Warfarin	607 (31.7)	300 (31.0)	307 (32.3)	0.53

* Indicates portion of data missing (from total n=1916). Chronic heart failure duration, 192 (10.0%); prior chronic heart failure hospitalisation, 208 (10.9%); NYHA heart failure class, 5 (0.3%); systolic blood pressure (mm Hg), 97 (5.1%); body mass index, 60 (3.1%); potassium (mEq/L), 260 (13.6%); haemoglobin, 285 (14.9%); QRS duration, 85 (4.4%).

eGFR, estimated glomerular filtration rate; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association.

Rates of delivered shocks/ATPs therapies by baseline glomerular filtration rate among participants with a primary prevention implantable cardioverter defibrillator

Categories of estimated glomerular filtration rate (mL/min/1.73 m ²)	Patients (n)	Total person-years	Total number of shocks/ATPs therapies delivered	Patients who had no shock/ATP therapies, n (row %)	Patients who had at least one shock/ATP therapies, n (row %)	Patients who had at least one shock/ATP therapies inappropriate, n (row %)	Number of patients who had at least one shock/ATP therapies appropriate, n (row %)
Overall	1916	4329.38	1717	1400 (73.1)	516 (26.9)	187 (9.8)	351 (18.3)
90	173	387.18	175	119 (68.8)	54 (31.2)	20 (11.6)	35 (20.2)
60–89	794	1854.96	781	562 (70.8)	232 (29.2)	91 (11.5)	159 (20.0)
45–59	482	1080.37	403	361 (74.9)	121 (25.1)	37 (7.8)	82 (17.0)
<45	467	1006.88	358	358 (46.7)	109 (23.3)	39 (8.4)	75 (16.1)

ATP therapies, antiarrhythmia pacing.