

UCLA

UCLA Previously Published Works

Title

Prescription of Guideline-Recommended Implantable Cardioverter Defibrillator and Cardiac Resynchronization Therapy Among Patients Hospitalized With Heart Failure and Varying Degrees of Renal Function

Permalink

<https://escholarship.org/uc/item/8712f1v0>

Journal

The American Journal of Cardiology, 119(6)

ISSN

0002-9149

Authors

Pun, Patrick H
Sheng, Shubin
Sanders, Gillian
et al.

Publication Date

2017-03-01

DOI

10.1016/j.amjcard.2016.11.043

Peer reviewed



Published in final edited form as:

Am J Cardiol. 2017 March 15; 119(6): 886–892. doi:10.1016/j.amjcard.2016.11.043.

Prescription of Guideline-Recommended Implantable Cardioverter Defibrillator and Cardiac Resynchronization Therapy Among Patients Hospitalized with Heart Failure and Varying Degrees of Renal Function

Patrick H. Pun, MD MHS^{a,b}, Shubin Sheng, PhD^a, Gillian Sanders, PhD^a, Adam D. DeVore, MD^{a,c}, Daniel Friedman, MD^{a,c}, Gregg C. Fonarow, MD^d, Paul A. Heidenreich, MD, MS^e, Clyde W. Yancy, MD, MSc^f, Adrian F. Hernandez, MD^{a,c}, and Sana M. Al-Khatib, MD MHS^{a,c}

^aDuke Clinical Research Institute, Durham, NC

^bDepartment of Medicine, Division of Nephrology, Duke University School of Medicine, Los Angeles, CA

^cDepartment of Medicine, Division of Cardiology, Duke University School of Medicine, Los Angeles, CA

^dAhmanson-UCLA Cardiomyopathy Center, Ronald Reagan-UCLA Medical Center, Los Angeles, CA

^eW, Palo Alto, CA

^fDivision of Cardiology, Northwestern University, Feinberg School of Medicine, Chicago, IL

Abstract

Implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT) reduce mortality in many patients with heart failure (HF), but the current use and effectiveness of ICD/CRT in patients with chronic kidney disease (CKD) are uncertain. We examined associations between kidney function and guideline-recommended prescription of ICD/CRT in the Get With The Guidelines-Heart Failure registry, a performance improvement program for hospitalized HF patients. We compared differences in ICD and CRT prescription between the following categories of estimated glomerular filtration rate (eGFR) (mL/min/1.73 m²): ≥60, 59–30, <30, and dialysis-dependent. From 2008 through 2014, 26,286 patients were eligible for ICD or CRT, and 16,123 (61%) had an eGFR <60. De novo ICD and CRT prescription in this group was low at 45% and 30.5%, respectively. Compared to patients with eGFR ≥60, patients with eGFR 30–59 were more likely to receive an ICD (adjusted odds ratio [aOR]=1.08, 95% confidence intervals [CI] 1.01–1.14), while dialysis patients were less likely (aOR=0.61, 95% CI 0.5–0.76). Worse kidney function was associated with a decreased likelihood of CRT prescription (aOR=0.97 per 10

Corresponding Author: Patrick Pun, MD MHS; PO Box 17696 Durham, NC, 27715 Patrick.Pun@dm.duke.edu; Tel: 919-668-8993; Fax 919-668-7032.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

mL/min eGFR decrease, $p=0.03$). During the study period, the likelihood of both ICD and CRT prescription increased over time among CKD patients (ICD aOR=1.12(95%CI 1.07–1.18), CRT aOR=1.14(95%CI 1.06–1.23) per year). Prescription of an ICD/CRT was associated with greater one-year survival in all eGFR groups. In conclusion, there are significant CKD-based differences in prescription of ICD and CRT in HF. However, given the current state of evidence, it is unclear whether or not improved prescription of ICD and CRT in the CKD population will result in improvement in outcomes.

Keywords

chronic kidney disease; congestive heart failure; arrhythmias

Introduction

Heart failure (HF) and chronic kidney disease (CKD) are highly coincident conditions; more than one-third of all patients with HF also have CKD.¹ Despite the fact that the presence of CKD independently predicts increased mortality and morbidity, HF patients with CKD are less likely to be provided with guideline-recommended HF medications, perhaps due to uncertainty regarding the benefit and risk of interventions in this patient population.^{2–4} Implantable cardioverter defibrillators (ICD) and cardiac resynchronization therapy (CRT) devices are therapies that reduce mortality in many patients with HF.⁵ Among patients with moderate to advanced CKD, a growing body of evidence suggests that ICD therapy is associated with a reduced or absent mortality benefit; however, current practice guidelines do not make specific provisions for the consideration of CKD in the decision to implant these devices.^{6–9} Given the uncertainty regarding the effectiveness and potential risks with use of ICD/CRT in this population, we conducted this study in order to: 1) examine whether or not rates of guideline-recommended device prescription and use vary according to the presence and severity of CKD, and 2) evaluate temporal trends in prescription of ICD/CRT in HF patients with CKD.

Methods

Data for this study were obtained from the Get With The Guidelines-Heart Failure (GWTG-HF) database. The GWTG-HF program was established as a quality improvement initiative that involves data collection on patients hospitalized for HF as previously described.¹⁰ Adult patients hospitalized with an episode of new or worsening HF as the primary reason for admission, or patients with significant HF symptoms that developed during hospitalization in which HF was the primary discharge diagnosis are eligible for the GWTG-HF registry. Data collected include patient demographics, clinical characteristics, prior therapies and interventions, in-hospital outcomes, and contraindications to evidence-based therapies. Specific data are collected regarding the eligibility for ICD/CRT, presence of an ICD/CRT on admission, any ICD/CRT implantation during the index hospitalization or scheduled outpatient implantation at the time of discharge, and documented contraindications to ICD/CRT implantation. Patient variables used for this study included demographic characteristics, hospital-reported medical history, left ventricular ejection fraction(LVEF),

QRS duration on admission ECG, admission vital signs, chronic dialysis-dependency at enrollment, and admission serum creatinine values. Data quality is ensured by data checks to prevent out-of-range entries and periodic data audits.

Because the data are used primarily at the local site for quality improvement, institutions participating in GWTG-HF are granted a waiver of informed consent under the Common Rule. Quintiles (Cambridge, MA) served as the registry coordinating center, and the Duke Clinical Research Institute (Durham, NC) served as the data analysis center. Hospital data elements are collected for all enrolling hospitals from the American Hospital Association database. The Institutional Review Board of the Duke University Health System approved this study.

We selected patients who were hospitalized for HF between February 2008 and December 2014 and had available data on admission serum creatinine. Patients who did not survive to hospital discharge or were discharged to somewhere other than home were excluded. Additionally, patients with physician-documented contraindications to primary prevention ICD implantation including LVEF<35%, class IV heart failure symptoms, myocardial infarction <40 days prior to implant, coronary artery bypass surgery <90 days prior to implant, not on optimal medical therapy, and new-onset HF (<3 months) were excluded, consistent with clinical guidelines.¹¹ For the CRT analyses, we used a QRS duration of 150ms to determine patients who would be eligible for a guideline-recommended CRT (CRT with ICD or CRT pacemaker). A QRS cutoff of 150 ms was chosen because the evidence on efficacy of CRT from randomized clinical trials is strongest in these patients, and current guidelines designate CRT as a class I indication in patients with a QRS 150 ms and left bundle branch block and as a class IIa indication in patients with a QRS 150 ms and non-left bundle branch block morphology.¹¹

The primary outcome was documented prescription of a de-novo ICD or CRT, either placed during hospitalization or planned to be placed following discharge. In a sensitivity analysis, we also included patients who had a pre-existing ICD or CRT prior to hospitalization to assess the prevalent use of guideline-based ICD/CRT by kidney function. As a secondary outcome, we examined the association between device prescription and one-year mortality among eGFR groups. Using linkage to GWTG-HF, mortality data were obtained from the Center for Medicare Services (CMS) claims database with indirect identifiers as described previously.¹²

Estimated glomerular filtration rate (eGFR) at admission was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.¹³ For consistency with prior literature, patients were then grouped into the following categories of estimated GFR (in mL/min per 1.73 m²): 60, 59–30, <30 but not receiving dialysis, and dialysis-dependent. Because serum creatinine levels at admission for HF may not be at steady state due to acute kidney injury, we also performed a sensitivity analysis utilizing the discharge serum creatinine to determine eGFR categories. Baseline characteristics were compared between the eGFR groups. Differences in baseline characteristics and outcomes between groups were assessed using the Kruskal-Wallis and Pearson χ^2 tests as appropriate. Multivariable logistic regression models using generalized estimating equations to account for in-hospital

clustering was performed to determine odds ratios for receiving a device within each eGFR stratum compared with the ≥ 60 group, utilizing baseline variables significantly associated with outcome ($p < 0.05$) in adjusted models or variables thought to be clinically relevant to outcome. Multiple imputation was used to impute missing data for covariates; less than 2% missingness was observed for all variables used in the multivariable models. Temporal trends in ICD/CRT prescription were assessed using Cochran-Armitage tests. Finally, multivariable logistic regression models were performed to determine baseline variables that were independently associated with device prescription among patients with $eGFR < 60$. A two-sided $p < 0.05$ was considered statistically significant. Analyses were performed with SAS software version 9.2 (SAS Institute, Cary, NC).

Results

Between February 2008 and December 2014, there were 310,468 patients hospitalized with HF across 357 inpatient facilities. We excluded 185,253 (59.7%) with $LVEF > 35\%$ or with missing data on LVEF, 33,678 (10.8%) with new-onset HF or missing data on HF history, and 22,339 (7.2%) patients who did not survive to hospital discharge or were discharged to somewhere other than home. 17,157 patients (5.5%) were excluded due to missing data on admission serum creatinine or dialysis history. The final ICD-eligible and CRT-eligible cohorts were determined from the remaining 52,041 patients with $LVEF \geq 35\%$. (Figure 1A/B) 61.3% of patients eligible for guideline-based ICD or CRT had evidence of kidney disease with an $eGFR < 60$. Demographic and clinical characteristics of the ICD-eligible cohort and CRT-eligible cohorts grouped by baseline eGFR status are shown in Table 1 and 2.

Figure 2 shows the rates of de-novo ICD and CRT prescription in eligible patients by eGFR group. 45% of all eligible patients with $eGFR < 60$ received a de novo ICD, and only 30.5% of CRT-eligible CKD patients received a de novo CRT. Patients with an $eGFR 59-30$ had a slightly higher rate of ICD prescription compared to patients with $eGFR \geq 60$ (46% vs 44%, $p < 0.0001$), whereas patients on dialysis had a much lower rate of prescription (32%, $p < 0.0001$). CRT prescription rates were progressively lower with lower eGFR (p -value for trend < 0.0001).

After adjustment for baseline covariates, dialysis patients were the least likely to receive an ICD compared with patients with an $eGFR \geq 60$ (aOR=0.61, 95% CI 0.5–0.76, $p < 0.0001$) (Table 3). In contrast, patients with an $eGFR 59-30$ were more likely to receive a guideline-recommended ICD compared with patients with preserved renal function (aOR=1.08, 95% CI 1.01–1.14, $p = 0.02$). For CRTs, after adjustment for baseline differences there was a trend towards decreased likelihood of CRT prescription among all eGFR groups < 60 compared with the $eGFR \geq 60$ group, but the relationship was significant only for patients with $eGFR < 30$ not on dialysis. However, eGFR was significantly associated with CRT prescription when examined as a continuous variable (aOR=0.97 per 10 decrease in eGFR, $p = 0.03$).

The rate of ICD prescription increased over time for all non-dialysis patients, but was most pronounced among patients with an $eGFR 59-30$ (29% in 2008 to 52% in 2014, p -value for

trend <0.0001) (Figure 3). ICD prescription also increased among chronic dialysis patients from 16% in 2008 to 42% in 2012, but subsequently declined to 33% in 2014 (p=0.0019). There were no significant time trends in CRT prescription among patients with eGFR<60 (Figure 4).

We examined the robustness of our study findings in 3 sensitivity analysis models (Supplemental Table 1). First, we used discharge creatinine measurements to determine eGFR given the possibility of misclassification using admission creatinine. The overall patterns of ICD and CRT prescription by eGFR group remained unchanged. Second, we included patients with pre-existing ICD and CRT devices at hospital admission to assess prevalent and incident device use. The overall pattern of ICD use or prescription among CKD patients also remained the same. For CRT devices, prescription among patients with eGFR<30 was increased, but otherwise findings in other eGFR groups remained unchanged. Finally, we used expanded QRS duration criteria (≥ 120 ms) suggested by 2012 update of device-based therapy guidelines as a class IIa recommendation for CRT prescription.¹¹ Only 29% in the overall cohort were prescribed a CRT due to the increased number of eligible patients. There was no change in the pattern of progressively declining CRT prescription with lower eGFR.

22.9% of the cohort had available mortality data via linkage to CMS claims data. In this limited analysis, one-year mortality progressively increased with CKD severity, and was more than two-fold higher among dialysis patients compared to patients with eGFR ≥ 60 (unadjusted HR=2.8, 95% CI 2.1–4.0) (Supplemental Table 2). Comparison of mortality rates between device-eligible patients who were prescribed versus not prescribed ICD or CRT devices showed increased survival among those who were prescribed devices in all eGFR subgroups; the survival advantage was more pronounced among patients prescribed CRT devices.

Discussion

In this large population of hospitalized patients with HF, we examined guideline-recommended ICD and CRT prescription among eligible patients across categories of kidney function. We found that CKD was highly prevalent among patients with HF, with more than 60% of all patients having an eGFR<60. ICD/CRT prescription was low among patients with CKD. Compared with patients without significant CKD, guideline-recommended ICD prescription was higher among patients with moderate CKD and significantly lower among patients on dialysis. In contrast, guideline recommended CRT prescription declined progressively with lower levels of kidney function. Sensitivity analyses using discharge serum creatinine to determine kidney function, accounting for devices present during hospital admission, and using less a less stringent QRS criterion for CRT eligibility did not substantially alter the trends observed in the primary analysis. In a limited analysis of mortality rates, we found that prescription of devices appeared to be associated with a survival advantage, particularly for CRT prescription. Our analysis of temporal prescription trends showed an increasing rates of prescription of both ICD and CRT among CKD patients.

Previous studies have suggested that guideline-recommended therapies for HF are less likely to be used in patients with CKD. In a prior study of the GWTG-HF registry, lower eGFR was associated with lower usage rates of beta-blockers, ACEI/ARB, and anticoagulation for atrial fibrillation.² A more recent study of HF patients receiving care at outpatient cardiology clinics examined adherence to 7 guideline-recommended therapies among CKD patients, including ICD/CRT use.⁴ The authors found no independent association between prescription of ICD or CRT and kidney function, although the lack of association could be explained by insufficient statistical power given the smaller size of the ICD/CRT-eligible cohort (6,383 patients ICD-eligible and 1,263 patients CRT-eligible) in that study. Several potential factors may explain the apparent eGFR-based differences observed in our study. First, differences in prescription may reflect physician attitudes towards certain CKD subgroups based on perceptions of risk/benefit and the current state of evidence. Increased prescription of ICD among patients with moderate CKD might be related to a perception of increased risk with an increased burden of ischemic heart disease and sudden cardiac death (SCD) in these patients. Lower prescription of ICD among more advanced CKD patients including dialysis patients could be related to the higher rates of complications, and concern for lack of benefit due to competing risks of non-arrhythmic death. Overall, concerns for increased risks of device-related complications and the lack of strong evidence supporting the benefit of ICD/CRT in patients with more advanced CKD may have influenced physicians' decisions not to follow guideline recommendations. Second, patients may also differ in preferences for implantable device therapy due to the high burden of co-morbidities and invasive procedures already borne by this patient population, particularly among patients receiving chronic dialysis.¹⁴

Patients with CKD are at a markedly increased risk of SCD. The risk of SCD is two-fold greater among patients with an eGFR 15–59 compared to with an eGFR \geq 60, and chronic dialysis patients are among the highest risk groups for SCD with an annual rate of 6%.^{15–17} Although ICD are proven to reduce SCD and overall mortality in selected populations, the role of these devices in patients with CKD remains unclear, since patients with advanced CKD have been excluded from previous clinical trials and higher risks of competing causes of death may limit device efficacy. A meta-analysis of 3 randomized trials of primary prevention ICD found no significant mortality benefit among patients with an eGFR < 60.⁹ A recent analysis found no significant survival advantage among dialysis patients who received guideline-recommended primary prevention ICD compared to propensity-matched dialysis patients with HF.⁸ Adding to the uncertainty surrounding the role of ICD among CKD patients are potential safety concerns including an increased rate of implantation-related and infectious ICD complications.^{18,19} While these data should be confirmed in randomized controlled trials, the current available evidence may not support the increased utilization of ICD in patients with moderate CKD (eGFR 30–59) relative to patients with less severe CKD that was observed in our study.

CRT in reduced ejection fraction patients with evidence of electric dyssynchrony is associated with improvement in LVEF, reduced risk of ventricular arrhythmia and improvement in HF symptoms.²⁰ Secondary analyses of CRT trials examining outcomes among patients with mild to moderate CKD have reported similar benefits compared to those observed in HF patients without CKD, but with higher rates of complications.^{21,22} A recent retrospective

study evaluating the comparative effectiveness of CRT with ICD versus ICD alone in CRT-eligible patients found a lower risk of death or HF hospitalization among patients with moderate-to-severe CKD.²³ Other observational studies of CKD patients have noted significant improvements in renal function among patients who received a CRT-D versus those who received an ICD alone.^{24,25} Taken together, these findings suggest that the underutilization of guideline-recommended CRT among patients with CKD observed in our study may not be justified; thus, our study findings may highlight an important opportunity to improve care and outcomes for CKD patients.

Several limitations should be considered in interpreting this study's findings. First, contraindications to therapy were recorded as documented in the medical record and may have been underreported. We did not have information on several important variables including New York Heart Association functional classification and electrocardiographic data such as left bundle branch morphology; both are factors that might have influenced guideline-based treatment decisions. Second, creatinine measurement at hospital admission may not reflect steady state conditions, leading to misclassification of chronic kidney disease status. To address this limitation, we performed a sensitivity analysis using the discharge serum creatinine to determine eGFR which did not show any substantial changes from the primary analysis, decreasing the likelihood of misclassification bias. Third, hospitals enrolled in the GWTG-HF program might have a higher likelihood of following guideline-based recommendations, and thus our results may not be generalizable to overall community practice. Fourth, we do not have data on whether patients who were scheduled for planned device implantation after hospital discharge actually received prescribed devices; it is possible that these patients did not ultimately receive a prescribed device due to intervening illness or non-compliance. The primary purpose of our study was to evaluate guideline-based prescribing patterns rather than compliance with prescribed therapy, but we acknowledge that our results may over-report actual ICD/CRT usage. Fifth, we only had data on mortality for a proportion of the cohort and the results of our unadjusted mortality analysis may have been subject to selection bias and confounding. Lastly, residual measured and unmeasured confounding may have impacted some of our findings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This analysis was funded by the National Institute of Diabetes, Digestive and Kidney Diseases of the National Institutes of Health under Award Numbers P30DK096493 and 5K23DK098281 to Dr. Pun. The American Heart Association provides the Get With The Guidelines–Heart Failure (GWTG-HF) and has received funding in the past from Medtronic, GlaxoSmithKline, Ortho-McNeil and the American Heart Association Pharmaceutical Roundtable.

Conflict of Interest Disclosures:

Dr. DeVore reports research support from the American Heart Association, Amgen, and Novartis. Dr. Friedman reports educational grants from Boston Scientific and St. Jude Medical. Dr. Fonarow reports consultancy fees from Amgen, Baxter, Bayer, Janssen, Novartis, and Medtronic. All authors reviewed and approved the final manuscript.

References

1. Cannizzaro LA, Piccini JP, Patel UD, Hernandez AF. Device therapy in heart failure patients with chronic kidney disease. *J Am Coll Cardiol.* 2011; 58:889–896. [PubMed: 21851875]
2. Patel UD, Hernandez AF, Liang L, Peterson ED, LaBresh KA, Yancy CW, Albert NM, Ellrodt G, Fonarow GC. Quality of care and outcomes among patients with heart failure and chronic kidney disease: A Get With the Guidelines -- Heart Failure Program study. *Am Heart J.* 2008; 156:674–681. [PubMed: 18946892]
3. Fonarow GC, Yancy CW, Albert NM, Curtis AB, Stough WG, Gheorghiade M, Heywood JT, McBride ML, Mehra MR, O'Connor CM, Reynolds D, Walsh MN. Heart failure care in the outpatient cardiology practice setting: findings from IMPROVE HF. *Circ Heart Fail.* 2008; 1:98–106. [PubMed: 19808279]
4. Heywood JT, Fonarow GC, Yancy CW, Albert NM, Curtis AB, Stough WG, Gheorghiade M, McBride ML, Mehra MR, O'Connor CM, Reynolds D, Walsh MN. Influence of renal function on the use of guideline-recommended therapies for patients with heart failure. *Am J Cardiol.* 2010; 105:1140–1146. [PubMed: 20381667]
5. Russo AM, Stainback RF, Bailey SR, Epstein AE, Heidenreich PA, Jessup M, Kapa S, Kremers MS, Lindsay BD, Stevenson LW. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation appropriate use criteria task force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. *Heart rhythm : the official journal of the Heart Rhythm Society.* 2013; 10:e11–e58.
6. Pun PH. The interplay between CKD, sudden cardiac death, and ventricular arrhythmias. *Adv Chronic Kidney Dis.* 2014; 21:480–488. [PubMed: 25443573]
7. Hess PL, Hellkamp AS, Peterson ED, Sanders GD, Al-Khalidi HR, Curtis LH, Hammill BG, Pun PH, Curtis JP, Anstrom KJ, Hammill SC, Al-Khatib SM. Survival after primary prevention implantable cardioverter-defibrillator placement among patients with chronic kidney disease. *Circ Arrhythm Electrophysiol.* 2014; 7:793–799. [PubMed: 25038119]
8. Pun PH, Hellkamp AS, Sanders GD, Middleton JP, Hammill SC, Al-Khalidi HR, Curtis LH, Fonarow GC, Al-Khatib SM. Primary prevention implantable cardioverter defibrillators in end-stage kidney disease patients on dialysis: a matched cohort study. *Nephrol Dial Transplant.* 2015; 30:829–835. [PubMed: 25404241]
9. Pun PH, Al-Khatib SM, Han JY, Edwards R, Bardy GH, Bigger JT, Buxton AE, Moss AJ, Lee KL, Steinman R, Dorian P, Hallstrom A, Cappato R, Kadish AH, Kudenchuk PJ, Mark DB, Hess PL, Inoue LY, Sanders GD. Implantable Cardioverter-Defibrillators for Primary Prevention of Sudden Cardiac Death in CKD: A Meta-analysis of Patient-Level Data From 3 Randomized Trials. *Am J Kidney Dis.* 2014; 64:32–39. [PubMed: 24518128]
10. Smaha LA, American Heart A. The American Heart Association Get With The Guidelines program. *Am Heart J.* 2004; 148:S46–S48. [PubMed: 15514634]
11. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO. American College of Cardiology F, American Heart Association Task Force on Practice G, Heart Rhythm S. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation.* 2013; 127:e283–e352. [PubMed: 23255456]
12. Hammill BG, Hernandez AF, Peterson ED, Fonarow GC, Schulman KA, Curtis LH. Linking inpatient clinical registry data to Medicare claims data using indirect identifiers. *Am Heart J.* 2009; 157:995–1000. [PubMed: 19464409]
13. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *Am J Kidney Dis.* 2010; 55:622–627. [PubMed: 20338463]

14. Pun PH, Schumm D, Sanders GD, Hickey D, Middleton JP, Clapp-Channing N, Al-Khatib SM. A pilot study using an implantable device to characterize cardiac arrhythmias in hemodialysis patients: implications for future research. *Ann Noninvasive Electrocardiol.* 2012; 17:159. [PubMed: 22537338]
15. Pun PH, Smarz TR, Honeycutt EF, Shaw LK, Al-Khatib SM, Middleton JP. Chronic kidney disease is associated with increased risk of sudden cardiac death among patients with coronary artery disease. *Kidney Int.* 2009; 76:652–658. [PubMed: 19536082]
16. USRDS Annual Data Report. Atlas of End-Stage Renal Disease in the United States. 2015
17. Passman R, Herzog CA. End-stage renal disease: sudden cardiac death: stratifying risk in dialysis patients. *Nat Rev Nephrol.* 2011; 7:133–135. [PubMed: 21151208]
18. Dasgupta A, Montalvo J, Medendorp S, Lloyd-Jones DM, Ghossein C, Goldberger J, Passman R. Increased complication rates of cardiac rhythm management devices in ESRD patients. *Am J Kidney Dis.* 2007; 49:656–663. [PubMed: 17472848]
19. Buiten MS, De Bie MK, Van Der Heijden AC, Rotmans JJ, Bootsma M, Marc Groeneveld JH, Wolterbeek R, Rabelink TJ, Jukema JW, Schalij MJ, Van Erven L. Chronic kidney disease and implantable cardioverter defibrillator related complications: 16 years of experience. *J Cardiovasc Electrophysiol.* 2014; 25:998–1004. [PubMed: 24758287]
20. Boriani G, Savelieva I, Dan GA, Deharo JC, Ferro C, Israel CW, Lane DA, La Manna G, Morton J, Mitjans AM, Vos MA, Turakhia MP, Lip GY. Document r. Chronic kidney disease in patients with cardiac rhythm disturbances or implantable electrical devices: clinical significance and implications for decision making—a position paper of the European Heart Rhythm Association endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society. *Europace.* 2015; 17:1169–1196. [PubMed: 26108808]
21. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L. Cardiac Resynchronization-Heart Failure Study I. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med.* 2005; 352:1539–1549. [PubMed: 15753115]
22. Garg N, Thomas G, Jackson G, Rickard J, Nally JV Jr, Tang WH, Navaneethan SD. Cardiac resynchronization therapy in CKD: a systematic review. *Clin J Am Soc Nephrol.* 2013; 8:1293–1303. [PubMed: 23660183]
23. Friedman DJ, Singh JP, Curtis JP, Tang WH, Bao H, Spatz ES, Hernandez AF, Patel UD, Al-Khatib SM. Comparative Effectiveness of CRT-D Versus Defibrillator Alone in HF Patients With Moderate-to-Severe Chronic Kidney Disease. *J Am Coll Cardiol.* 2015; 66:2618–2629. [PubMed: 26670062]
24. Hoke U, Khidir MJ, van der Velde ET, Schalij MJ, Bax JJ, Delgado V, Marsan NA. Cardiac Resynchronization Therapy in CKD Stage 4 Patients. *Clin J Am Soc Nephrol.* 2015; 10:1740–1748. [PubMed: 26408549]
25. Singal G, Upadhyay GA, Borgquist R, Friedman DJ, Chatterjee NA, Kandala J, Park MY, Orencole M, Dec GW, Picard MH, Singh JP, Mela T. Renal Response in Patients with Chronic Kidney Disease Predicts Outcome Following Cardiac Resynchronization Therapy. *Pacing Clin Electrophysiol.* 2015; 38:1192–1200. [PubMed: 26179289]

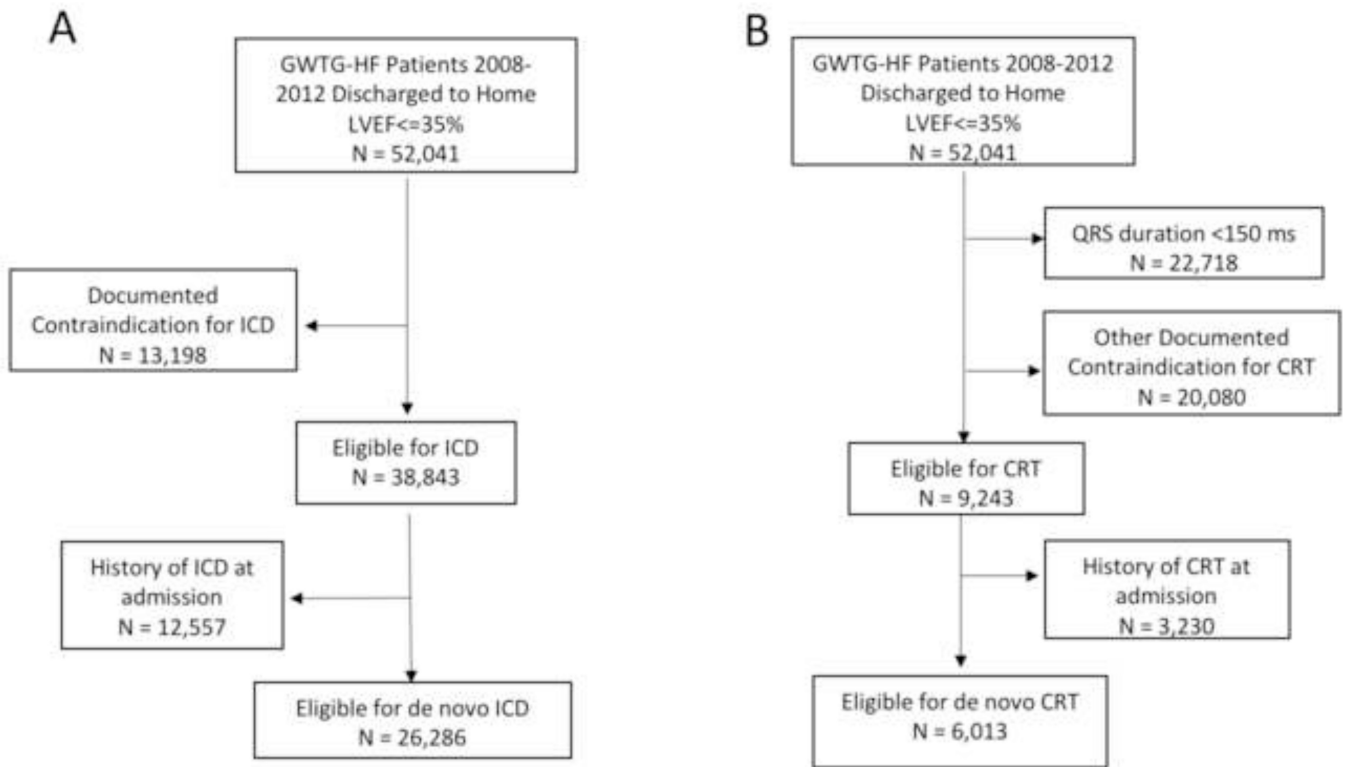


Figure 1.
A/B: Flowchart illustrating determination of ICD-eligible (A) and CRT-eligible (B) cohorts.

ICD and CRT Prescription by eGFR category

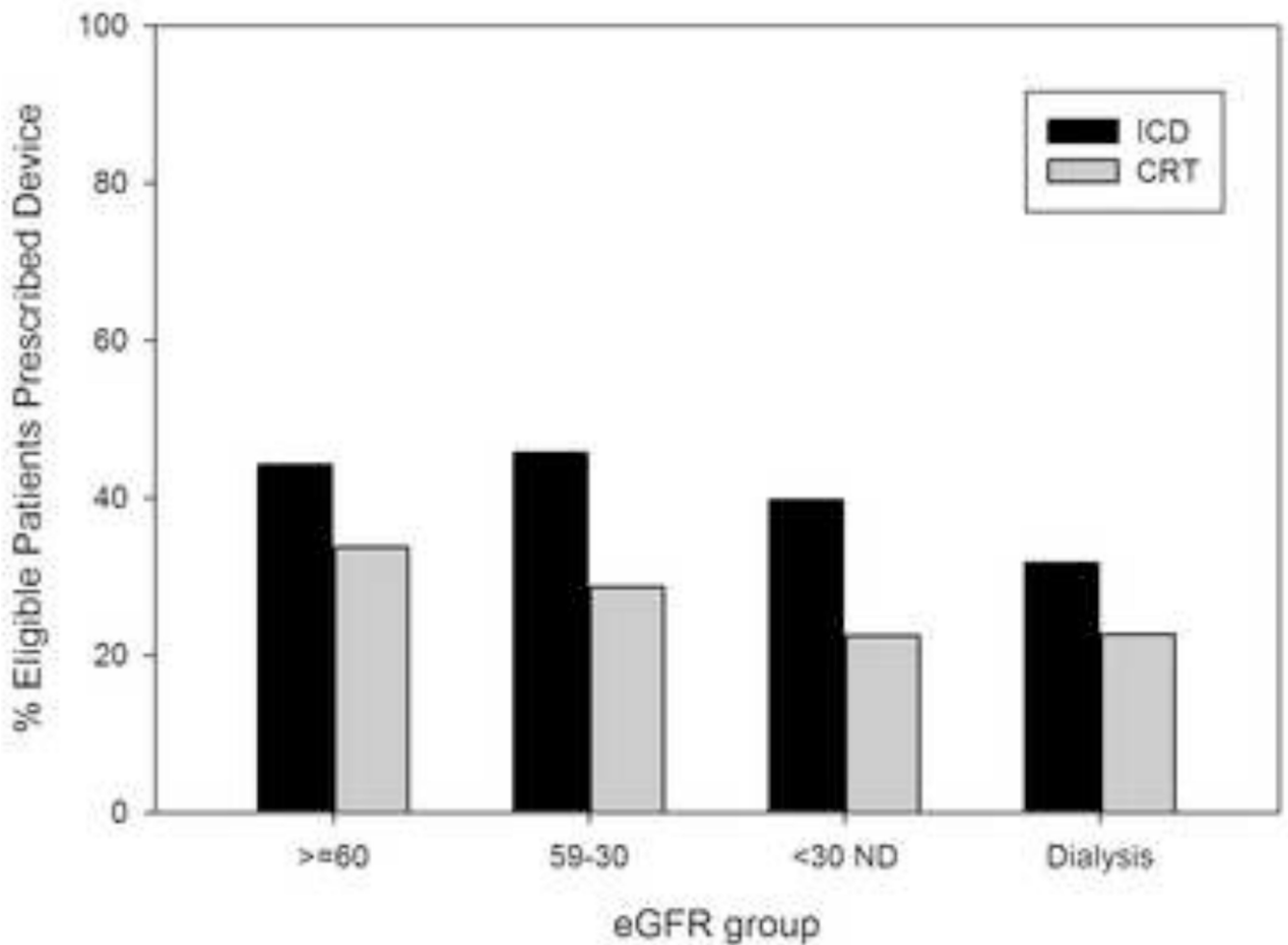


Figure 2.

ICD and CRT prescription by eGFR group. Compared with patients with a baseline eGFR ≥ 60 mL/min per 1.73 m², patients with an eGFR 59–30 mL/min per 1.73 m² had a slightly higher rate of ICD prescription (46% vs. 44%, $p < 0.0001$) whereas patients on dialysis had a much lower rate of prescription (32%, $p < 0.0001$). CRT prescription rates were progressively lower with lower eGFR ($p < 0.0001$ for CRT prescription by eGFR category.) (ND=non-dialysis)

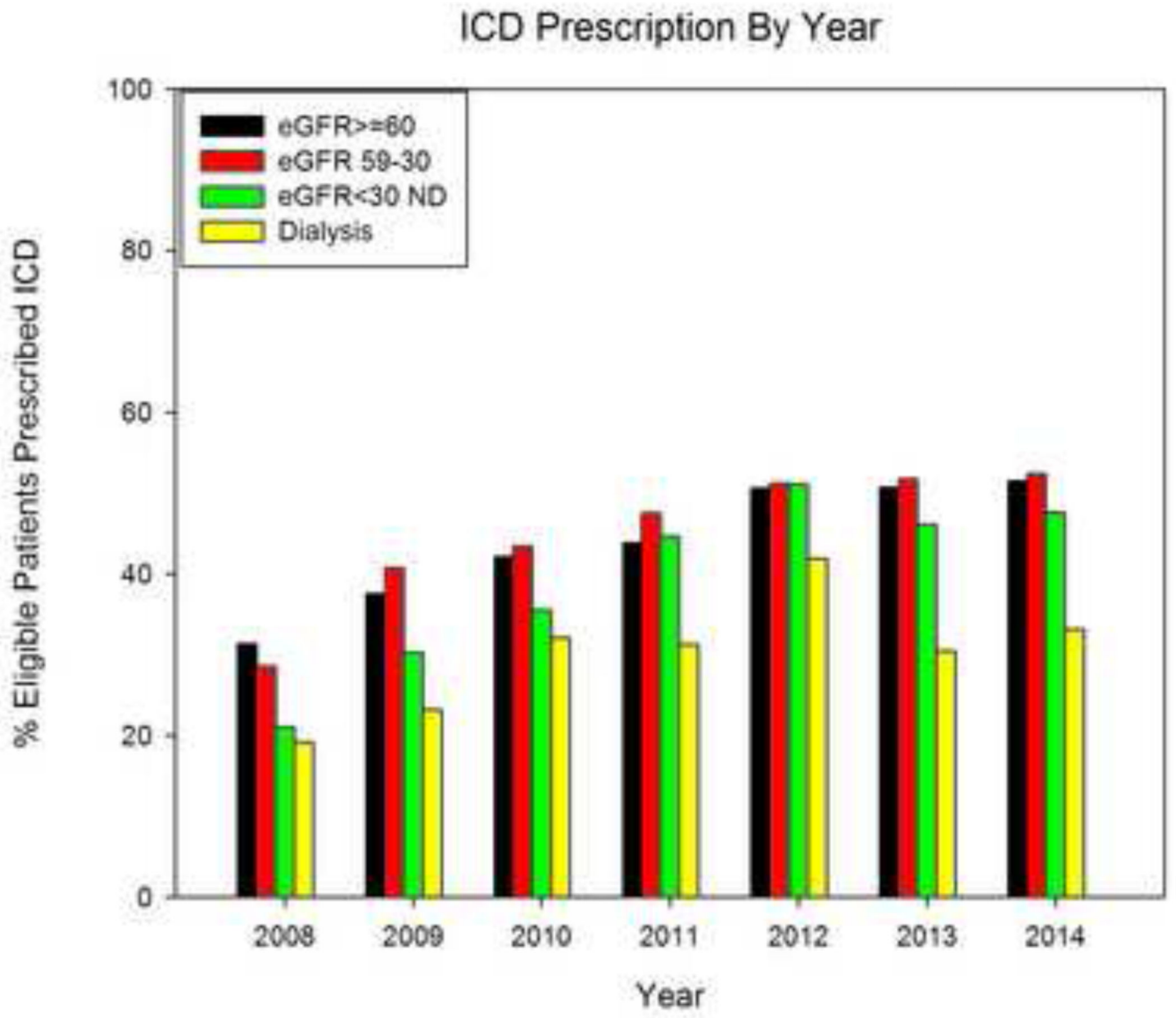


Figure 3. ICD prescription by eGFR group and admission year. (ND=non-dialysis)

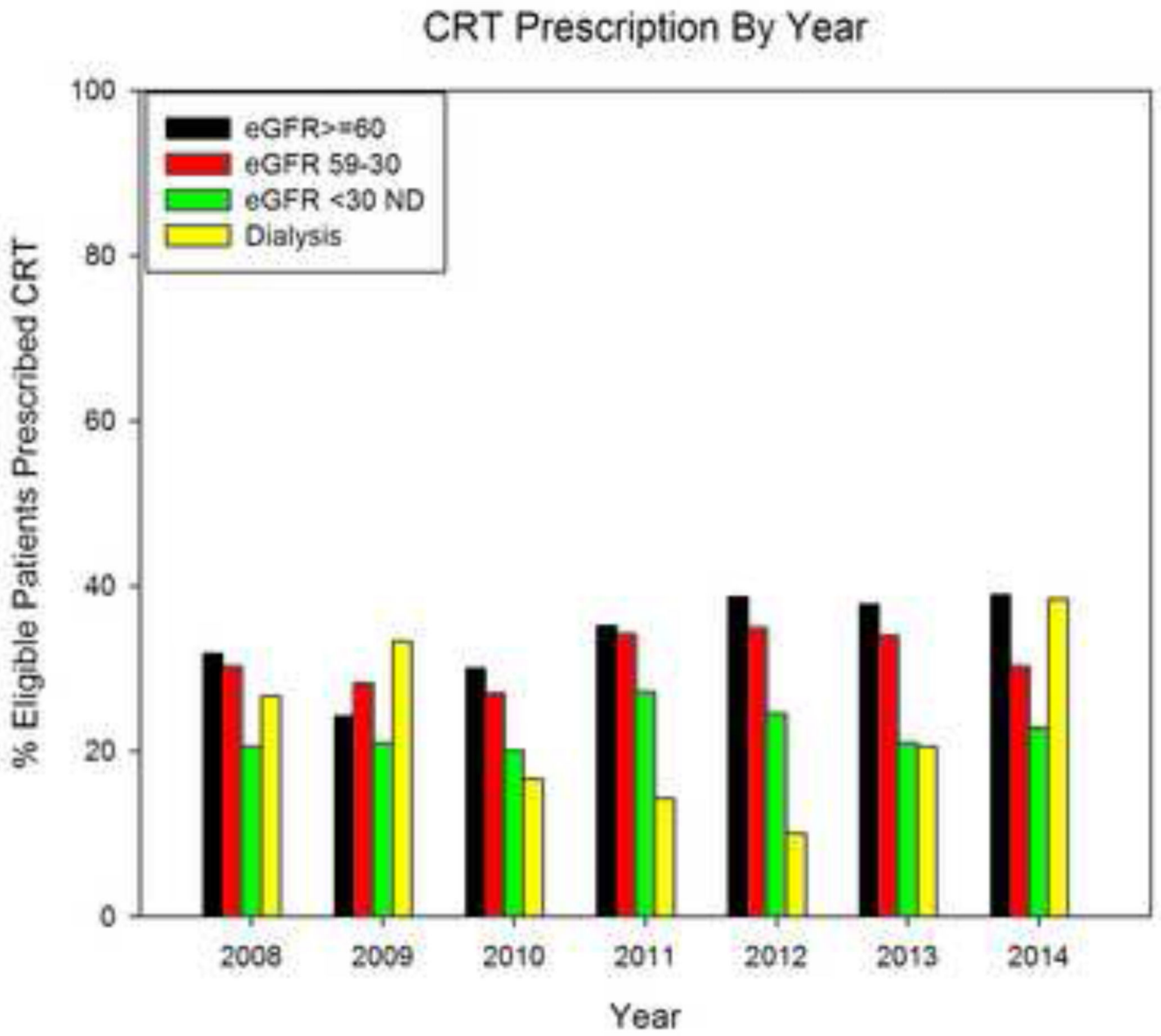


Figure 4. CRT prescription by eGFR group and admission year. (ND=non-dialysis)

Table 1

Baseline Characteristics of ICD-Eligible Patients by eGFR category

Variable	eGFR 60 (N=10153)	eGFR 30–59 (N=10958)	eGFR<30, not on dialysis (N=4112)	Dialysis (N=1063)	P-value
Demographics					
Age (Mean±SD)	61.1±14.6	71.7±12.6	73.3±12.6	64.7±14.3	<.0001
Women	30.9(%)	36.6(%)	41.3(%)	36.9(%)	<.0001
Black	33.1(%)	21.2(%)	20.2(%)	33.4(%)	<.0001
White	51.1(%)	65.1(%)	65.3(%)	47.4(%)	
Medical History					
Coronary artery disease	47.0(%)	59.6(%)	64.0(%)	59.2(%)	<.0001
Prior coronary artery bypass grafting	17.7(%)	27.5(%)	30.2(%)	24.1(%)	<.0001
Previous myocardial infarction	24.2(%)	29.1(%)	29.6(%)	26.6(%)	<.0001
Prior percutaneous intervention	17.7(%)	21.6(%)	21.6(%)	22.8(%)	<.0001
Hypertension	77.0(%)	79.1(%)	79.5(%)	83.9(%)	<.0001
Diabetes mellitus	39.2(%)	45.6(%)	52.4(%)	54.8(%)	<.0001
Atrial fibrillation	25.5(%)	37.7(%)	36.1(%)	23.4(%)	<.0001
Chronic obstructive pulmonary disease or asthma	31.6(%)	31.0(%)	29.1(%)	33.3(%)	0.012
Cerebral vascular accident/Transient ischemic attack	11.6(%)	15.0(%)	16.6(%)	18.0(%)	<.0001
Hyperlipidemia *	47.9(%)	55.8(%)	57.5(%)	49.5(%)	<.0001
Peripheral vascular disease	7.8(%)	13.1(%)	15.8(%)	18.5(%)	<.0001
Valvular heart disease	15.6(%)	19.5(%)	20.5(%)	16.9(%)	<.0001
Smoking	32.6(%)	16.3(%)	12.8(%)	21.0(%)	<.0001
Anemia *	9.8(%)	15.9(%)	25.8(%)	38.7(%)	<.0001
Ischemic history *	53.8(%)	67.0(%)	71.8(%)	65.2(%)	<.0001
Admission Variables (Mean ± SD)					
Body mass index (kg/m ²)	29.3±7.4	28.3±6.2	27.8±6.2	27.1±5.0	<.0001
Systolic blood pressure (mmHg)	135.6±27.2	133.0±27.1	133.1±28.7	143.2±31.3	<.0001
Diastolic blood pressure (mmHg)	82.9±18.8	77.8±17.9	75.3±17.8	80.5±20.4	<.0001
Serum creatinine (mg/dL)	1.0±0.2	1.5±0.3	5.7±23.7	7.4±33.0	<.0001

Variable	eGFR 60 (N=10153)	eGFR 30–59 (N=10958)	eGFR<30, not on dialysis (N=4112)	Dialysis (N=1063)	P-value
Blood urea nitrogen (mg/dL)	18.4±8.3	29.6±11.7	52.5±22.2	46.6±24.7	<.0001
eGFR on admission	83.5±29.5	45.0±4.3	21.1±6.8	N/A	<.0001
QRS duration on admission electrocardiogram	121.9±0.0	133.1±0.0	135.6±0.0	118.9±25.5	<.0001

* History of anemia and history of hyperlipidemia were determined at the discretion of hospital staff. Ischemic history is a composite of medical history of coronary artery disease, prior CABG, Previous MI, prior PCI

Table 2

Baseline Characteristics of CRT-Eligible Patients by eGFR Category

	eGFR 60 (N=1942)	eGFR 30-59 (N=2838)	eGFR<30, not on dialysis (N=1054)	Dialysis (N=179)	P-value
Demographics					
Age (Mean±SD)	66.3±13.4	74.4±11.3	76.5±10.6	70.6±11.2	<.0001
Women	28.4(%)	31.0(%)	37.4(%)	32.4(%)	<.0001
Black	21.2(%)	12.8(%)	12.6(%)	19.0(%)	<.0001
White	66.2(%)	76.5(%)	75.1(%)	57.5(%)	
Medical History					
Coronary artery disease	55.4(%)	62.8(%)	69.3(%)	67.0(%)	<.0001
Prior coronary artery bypass grafting	24.6(%)	33.2(%)	37.8(%)	29.6(%)	<.0001
Previous myocardial infarction	24.8(%)	28.8(%)	33.6(%)	30.2(%)	<.0001
Prior percutaneous intervention	19.5(%)	22.9(%)	21.9(%)	23.5(%)	0.045
Hypertension	75.4(%)	76.0(%)	76.5(%)	78.8(%)	0.8743
Diabetes mellitus	38.6(%)	43.3(%)	47.4(%)	58.1(%)	<.0001
Atrial fibrillation	30.5(%)	41.0(%)	43.6(%)	30.2(%)	<.0001
Chronic obstructive pulmonary disease or asthma	27.5(%)	29.1(%)	28.7(%)	28.5(%)	0.544
Cerebral vascular accident/Transient ischemic attack	11.8(%)	15.6(%)	16.7(%)	16.2(%)	0.0003
Hyperlipidemia *	53.6(%)	58.3(%)	57.1(%)	57.0(%)	0.0199
Peripheral vascular disease	8.1(%)	12.5(%)	16.4(%)	19.6(%)	<.0001
Valvular heart disease	16.2(%)	20.1(%)	24.1(%)	26.3(%)	<.0001
Smoking	23.9(%)	11.7(%)	10.0(%)	12.9(%)	<.0001
Anemia *	7.9(%)	14.2(%)	23.3(%)	34.1(%)	<.0001
Ischemic history *	61.9(%)	71.1(%)	78.0(%)	76.0(%)	<.0001
Admission Variables (Mean ± SD)					
Body mass index (kg/m ²)	28.4±6.5	27.9±5.8	27.4±5.5	27.4±5.3	0.0002
Systolic blood pressure (mmHg)	131.2±25.9	129.4±25.7	127.1±24.9	130.8±29.2	0.005
Diastolic blood pressure (mmHg)	78.1±16.6	74.4±15.5	71.5±14.9	71.9±17.1	<.0001
Serum creatinine (mg/dL)	1.0±0.2	1.5±0.2	5.0±18.1	5.0±2.7	<.0001

	eGFR 60 (N=1942)	eGFR 30-59 (N=2838)	eGFR<30, not on dialysis (N=1054)	Dialysis (N=179)	P-value
Blood urea nitrogen (mg/dL)	19.5±7.8	30.5±12.3	53.1±22.5	41.0±21.3	<.0001
eGFR on admission	79.6±26.9	44.5±4.3	21.6±6.6	N/A	<.0001
QRS duration on admission electrocardiogram	169.9±0.0	173.0±0.0	174.9±0.0	172.9±14.0	<.0001

* History of anemia and history of hyperlipidemia were determined at the discretion of hospital staff. Ischemic history is a composite of medical history of coronary artery disease, prior CABG, Previous MI, prior PCI

Table 3

Association between Baseline Kidney Function and Prescription of Implantable Cardioverter Defibrillator or Cardiac Resynchronization Therapy Among Eligible Patients*

eGFR (ml/min/1.75 m ²)	ICD Prescription		CRT Prescription	
	aOR=(95% CI)	P-value	aOR=(95% CI)	P-value
60	Reference		Reference	
59–30	1.08 (1.01–1.14)	0.02	0.92 (0.79–1.07)	0.28
<30 (not on dialysis)	0.97 (0.90–1.06)	0.53	0.80 (0.67–0.95)	0.01
On Dialysis	0.61 (0.50–0.76)	<.0001	0.69 (0.44–1.08)	0.1
Decrease (per 10 ml/min)	1.00 (0.99–1.01)	0.4501	0.97 (0.94–1.00)	0.03

* ICD analyses adjusted for admission year, age, gender, race, insurance status, cigarette smoking in the past year, systolic blood pressure on admission, history of anemia, ischemic heart disease, diabetes, hyperlipidemia, hypertension, atrial fibrillation, and hospital region. CRT analysis adjusted for significant factors in the final model that influenced CRT prescription including admission year, age, race, systolic blood pressure on admission, diabetes, and anemia due to decreased number of events.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript