ORIGINAL ARTICLE

Effect of cardiac resynchronization therapy on the risk of ventricular tachyarrhythmias in patients with chronic kidney disease

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Background: The effect of chronic kidney disease (CKD) on benefit from cardiac resynchronization therapy with defibrillator (CRT-D) in reducing ventricular tachyarrhythmia (VTA) risk among mild heart failure (HF) patients is not well understood.

Methods: We evaluated the impact of baseline renal function on VTAs in 1274 left bundle branch block (LBBB) patients enrolled in MADIT-CRT. Two prespecified subgroups were created based on estimated glomerular filtration rate (GFR): GFR <60 ($n = 413$) and GFR ≥ 60 ml/min/1.73 m² ($n = 861$). Primary end point was ventricular tachycardia/ventricular fibrillation/death (VT/VF/death). Secondary end points were any VT/VF and ventricular tachycardia ≥ 200 bpm or VF (fast VT/VF).

Results: There were 413 (32%) LBBB patients presenting with CKD, primarily of moderate severity (GFR mean 48.1 ± 8.3). For patients with and without CKD, CRT-D was associated with lower risk of the primary end point (GFR <60: HR = 0.61, 95% CI: 0.41–0.89, $p = .010$; GFR ≥ 60 : HR = 0.58, 95% CI: 0.52–0.89, $p = .005$), relative to ICD-only treatment. For patients in both renal function categories, CRT-D in comparison to ICD alone was associated with lower risk of VT/VF (GFR <60: HR = 0.68, 95% CI: 0.42–1.10, $p = .113$; GFR ≥ 60 : HR = 0.65, 95% CI: 0.48–0.88, $p = .005$) and fast VT/VF (GFR <60: HR = 0.49, 95% CI: 0.25–0.96, $p = .038$; GFR ≥ 60 : HR = 0.55, 95% CI: 0.39–0.80, $p = .001$), when accounting for competing mortality risk. This effect was independent of CRT-induced reverse remodeling.

Conclusion: Among mild HF patients with LBBB, those with and without CKD both derived benefit from CRT-D in risk reduction in VTAs, independent of cardiac reverse remodeling.

KEYWORDS

cardiac resynchronization therapy, chronic kidney disease, heart failure, ventricular tachyarrhythmias

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Chronic kidney disease (CKD), even before progression to dialysis, leads to increased risk of ventricular tachyarrhythmias (VTAs) and sudden cardiac death (SCD), an association that may be more pronounced in the setting of severe heart failure (HF) (Bonato, Lemos, Cassiolato, & Canziani, 2013; Chakko & Gheorghiade, 1985; Whitman, Feldman, & Deo, 2012). Cardiac resynchronization therapy (CRT) has been shown to decrease the risk of death and HF events in patients with diminished left ventricular (LV) function with prolonged QRS duration (Cleland et al., 2005; Linde et al., 2008; Moss et al., 2005, 2009). There is also evidence that CRT reduces the risk of developing VTAs (Arya et al., 2005; Barsheshet et al., 2011; Di Biase et al., 2008; Ermis et al., 2005). While renal function has been studied in association with the outcomes of death and HF among CRT patients, the effect of CKD on CRT-associated VTA risk reduction is not well understood, warranting further investigation (Daimee et al., 2015; Goldenberg et al., 2010; Lin et al., 2011; Van Bommel et al., 2011).

Accordingly, the aim of this study was to assess whether the presence of CKD at baseline modifies benefit from CRT in reducing the risk of ventricular tachycardia (VT) and ventricular fibrillation (VF) in mild HF patients with left bundle branch block (LBBB).

1 | METHODS

1.1 | Study population

The Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) has been detailed in prior publications (Moss et al., 2005, 2009). Briefly, 1820 patients with ischemic and nonischemic cardiomyopathy, LV ejection fraction $\leq 30\%$, QRS duration ≥ 130 ms, and New York Heart Association (NYHA) class I or II symptoms were randomly assigned to cardiac resynchronization therapy with defibrillator (CRT-D) versus implantable cardioverter-defibrillator (ICD)-only treatment in a 3:2 ratio. Optimal medical treatment for HF including beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers/angiotensin II inhibitors, diuretics, and statins was part of the therapy for all patients.

The 1820 patients were followed over an average duration of 2.4 years for the primary study at 110 centers in Europe, Israel, and North America, initially being seen at the 1-month mark and then at 3-month intervals after randomization. This study consisted of patients with left bundle branch block (LBBB), who comprised 1274 (70%) of the 1820 total patients in MADIT-CRT. Non-LBBB patients have been shown not to derive benefit from CRT-D and were thus not included in this study (Zareba et al., 2011). Analyses were performed on an intention-to-treat basis, with the initial treatment assignment applied.

1.2 | Device implantation and programming in MADIT-CRT

Patients in both CRT-D and ICD-only arms received commercially available Boston Scientific devices that were implanted using standard methods. Ventricular tachycardia (VT) and ventricular fibrillation (VF) therapy were approached using a two-zone configuration with the VT

zone set at 180 beats per minute (bpm) and VF zone set at 210 bpm. The VT zone first therapy involved burst-type antitachycardia pacing followed by biphasic shocks, as previously described (Levin et al., 2013).

1.3 | Definitions and end points

Baseline glomerular filtration rate (GFR) values were obtained using the following formula: $GFR = 186 \times \text{Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if African American})$. Two prespecified categories of patients were created based on estimated glomerular filtration rate (GFR): $GFR < 60 \text{ ml/min/1.73 m}^2$ and $GFR \geq 60 \text{ ml/min/1.73 m}^2$. CKD was defined as $GFR < 60 \text{ ml/min/1.73 m}^2$, in accordance with current guidelines and prior studies related to renal impairment (Daimee et al., 2015; Levin et al., 2013; Lin et al., 2011).

Furthermore, in a subanalysis, we performed a systematic evaluation of the CKD patients, and assessed the impact of the degree of renal insufficiency using intervals of $GFR = 15 \text{ ml/min/1.73 m}^2$. Accordingly, we evaluated CKD patients with $GFR \leq 45 \text{ ml/min/1.73 m}^2$ and $45 < GFR < 60 \text{ ml/min/1.73 m}^2$. Because there were 16 (0.9%) total patients and only seven LBBB patients with $GFR < 30 \text{ ml/min/1.73 m}^2$, specific subanalysis was not possible for patients with more severe renal dysfunction.

The primary end point of this study was the composite end point of first episode of any VT, VF, or all-cause mortality (any VT/VF/death). A composite end point was used to account for the competing risk of all-cause mortality. Secondary end points were first episode of any VT or VF (any VT/VF) and first episode of fast VT, defined as VT ≥ 200 bpm, or VF (fast VT/VF). The definition of fast VT was chosen based on the Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy (MADIT-RIT), which suggested that treating VTAs < 200 bpm may not be life saving (Moss et al., 2012). In MADIT-CRT, all VT and VF events were sustained, and treated with either antitachycardia pacing or shock. All end points were analyzed over an average follow-up period of 2.4 years in all LBBB patients by baseline GFR category.

An independent adjudication committee evaluated the stored electrograms of ICD and CRT-D devices. The definition of VT was set to a rate of 180–250 bpm if the rate of the ventricular electrograms (V) was greater than the rate of the atrial electrograms (A) and if 1:1 AV-conduction V-V changes were driving A-A changes. VF was defined as ventricular rate faster than 250 bpm with disorganized ventricular electrograms.

1.4 | Echocardiography methods

Echocardiograms were obtained before device implantation and at 1 year. Echocardiography investigators were qualified to perform echocardiography according to the approved protocol. Recordings were analyzed off-line at the Brigham and Women's Hospital, Boston, Massachusetts, at an independent echocardiography core laboratory. Echocardiography investigators who analyzed the images were blinded to treatment assignment or clinical outcome. Left ventricular

(LV) and left atrial (LA) volumes were measured by Simpson's disk method in the apical 4- and 2-chamber views and LVEF was calculated according to the established American Society of Echocardiography protocols (Lang et al., 2005).

1.5 | Statistical analysis

A comparison of baseline clinical characteristics between patients with $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ and $\text{GFR} \geq 60 \text{ ml/min/1.73 m}^2$ at enrollment was conducted using the chi-square test or Fisher's exact test for dichotomous variables and Wilcoxon signed-rank test for continuous variables.

The cumulative probabilities of any VT/VF/death, any VT/VF, and fast VT/VF by treatment arm within each renal function group were obtained using the Kaplan-Meier method. Log-rank test was used for comparisons of cumulative event rates.

Multivariable Cox proportional hazards regression analysis was used to assess the effect of CRT-D versus ICD-only treatment among LBBB patients receiving device therapy in each of the two renal function groups. Best subset selection was applied to candidate covariates, and the Cox model was adjusted for relevant covariates (CRT-D versus ICD-only treatment, ischemic cardiomyopathy, prior myocardial infarction, systolic blood pressure, weight, worst New York Heart Association heart failure stage, and current smoking). Interaction p -values between the CKD and non-CKD groups for CRT-D versus ICD-only effect were calculated and reported. For the end points of any VT/VF and fast VT/VF, Fine and Gray's extension of the Cox proportional hazards regression analysis was used in an attempt to account for the competing risk of all-cause mortality (Fine & Gray, 1999).

We additionally examined the relationship between CKD and the improvement in echocardiographic parameters of LV end-systolic volume (LVESV), LV end-diastolic volume (LVEDV), and LA volume (LAV) obtained at 1 year after CRT-D implantation.

All statistical tests were two sided, and a p -value $< .05$ was considered statistically significant. Analyses were conducted with SAS software (version 9.3, SAS institute, Cary, NC, USA).

2 | RESULTS

Among 1274 LBBB patients at enrollment in MADIT-CRT, there were 413 (32%) who presented with CKD, that is, $\text{GFR} < 60 \text{ ml/min/1.73 m}^2$ (mean 48.1 ± 8.3). In the CKD group, the following GFR range was observed: 1st quartile = 42.7, median = 49.5, 3rd quartile = 55.3. Thus, CKD patients in our study presented primarily with moderate renal impairment, as only seven (2%) LBBB patients had $\text{GFR} < 30 \text{ ml/min/1.73 m}^2$ as stated above.

The remaining 861 (68%) LBBB patients did not present with CKD and had $\text{GFR} \geq 60 \text{ ml/min/1.73 m}^2$ (mean 79.6 ± 16.0). For the non-CKD category, the following GFR range was found: 1st quartile = 67.8, median = 76.2, 3rd quartile = 87.7.

Baseline clinical characteristics by both CKD status and allocated treatment arms are shown in Table 1. Comparison of ICD and CRT-D

patients within a given GFR group was performed. No major differences were found between ICD and CRT-D patients within the two GFR groups.

Among those randomized to ICD, the primary end point of any VT/VF/death was observed in 61 (35%) patients with $\text{GFR} < 60$ and in 108 (31%) patients with $\text{GFR} \geq 60$. Any VT/VF was found in 36 (21%) patients with $\text{GFR} < 60$ and in 95 (28%) patients with $\text{GFR} \geq 60$. Fast VT/VF events occurred in 23 (13%) patients with $\text{GFR} < 60$ and in 68 (20%) patients with $\text{GFR} \geq 60$.

Among CRT-D recipients, any VT/VF/death was observed in 56 (23%) patients with $\text{GFR} < 60$ and in 123 (24%) patients with $\text{GFR} \geq 60$. Any VT/VF was found in 35 (15%) patients with $\text{GFR} < 60$ and in 103 (20%) patients with $\text{GFR} \geq 60$. Fast VT/VF events occurred in 17 (7%) patients with $\text{GFR} < 60$ and in 61 (12%) patients with $\text{GFR} \geq 60$.

2.1 | Effect of chronic kidney disease on benefit from CRT-D in reducing ventricular tachyarrhythmias

In patients with CKD, CRT-D was associated with a significantly lower probability of any VT/VF/death ($p = .007$, Fig. 1A), borderline-significant lower likelihood of any VT/VF ($p = .064$, Fig. 2A), and significantly lower incidence of fast VT/VF ($p = .034$, Fig. 2C). Multivariable analysis showed that patients with CKD receiving CRT-D experienced 39% significantly lower risk of any VT/VF/death ($p = .010$), 32% non-significant reduction in the risk of any first VT/VF ($p = .113$), and 51% significantly reduced risk of fast VT/VF ($p = .038$), relative to those receiving ICD only (Table 2).

Similarly, among patients without CKD at baseline, CRT-D versus ICD only was associated with a significantly lower probability of any VT/VF/death ($p = .006$, Fig. 1B), any VT/VF ($p = .004$, Fig. 2B), and fast VT/VF ($p < .001$, Fig. 2D). Multivariable analysis confirmed that CRT-D was associated with a 42% significant reduction in risk of any VT/VF/death ($p = .005$), 35% significantly lower risk of developing fast VT/VF ($p = .005$), and 45% significantly reduced risk of fast VT/VF ($p = .001$), when compared to ICD-only treatment, after accounting for the competing risk of mortality (Table 2).

2.2 | Effect of degree of renal insufficiency among chronic kidney disease patients on benefit from CRT-D in reducing ventricular tachyarrhythmias

We further evaluated the effect of degree of renal insufficiency on the primary end point. There were 141 patients with $\text{GFR} \leq 45$ and 272 patients with $45 < \text{GFR} < 60$. Among those with ICD, any VT/VF/death was observed in 23 (39%) patients with $\text{GFR} \leq 45$ and in 38 (47%) patients with $45 < \text{GFR} < 60$. Among CRT-D recipients, any VT/VF/death occurred in 19 (17%) patients with $\text{GFR} \leq 45$ and in 37 (24%) patients with $45 < \text{GFR} < 60$.

In those with $\text{GFR} \leq 45$, Kaplan-Meier analysis revealed that CRT-D was associated with a significantly lower probability of any VT/VF/death ($p = .034$). After multivariable adjustment, CRT-D was associated with a 64% significant reduction in risk of any VT/VF/

TABLE 1 Clinical characteristics of LBBB patients with GFR<60 and GFR≥60 at baseline, stratified by assigned treatment to ICD only or CRT-D

Clinical Characteristics	GFR < 60 ICD	GFR < 60 CRT-D	GFR ≥ 60 ICD	GFR ≥ 60 CRT-D
Number of patients	173	240	343	518
Female, no. (%)	61 (35)	85 (35)	94 (27)	152 (29)
Ischemic class I, no. (%)	22 (13)	20 (8)	38 (11)	61 (12)
Worst NYHA > 2 (>3 mos Prior), no. (%)	23 (14)	34 (15)	30 (9)	48 (10)
Prior CHF hospitalization, no. (%)	83 (50)	107 (45)	105 (31)	190 (37)
Prior CABG, no. (%)	52 (30)	65 (27)	60 (18)	102 (20)
Diabetes, no. (%)	76 (44)	83 (35)	84 (25)	141 (27)
Hypertension, no. (%)	130 (75)	164 (69)	203 (59)	305 (59)
Past atrial arrhythmias, no. (%)	27 (16)	29 (12)	42 (12)	43 (9)
Prior myocardial infarction, no. (%)	74 (44)	86 (37)	94 (28)	150 (30)
ACE inhibitor or ARB, no. (%)	163 (94)	226 (94)	334 (97)	502 (97)
Beta-blocker excl. Sotalol, no. (%)	156 (90)	222 (93)	328 (96)	491 (95)
Antiarrhy incl. amiodarone and sotalol, no. (%)	21 (12)	24 (10)	18 (5)	24 (5)
Diuretic, no. (%)	140 (81)	189 (79)	222 (65)	320 (62)
Age at enrollment, mean ± SD	69.2 ± 8.9	68.8 ± 9.4	62.1 ± 10.9	61.9 ± 10.9
QRS (ms), mean ± SD	162.3 ± 18.0	162.7 ± 19.1	165.1 ± 20.5	162.0 ± 18.8*
Heart rate (beats/min), mean ± SD	68.8 ± 11.0	67.2 ± 11.1	69.0 ± 11.5	68.0 ± 10.4
Body mass index, ^a mean ± SD	28.4 ± 4.9	27.8 ± 5.3	28.6 ± 5.3	28.9 ± 5.2
Blood urea nitrogen (mg/dl), mean ± SD	28.5 ± 10.5	28.0 ± 10.0	18.6 ± 6.0	17.9 ± 5.6
Creatinine (mg/dl), mean ± SD	1.46 ± 0.30	1.47 ± 0.30	0.99 ± 0.17	0.98 ± 0.17
BUN/Creatinine, mean ± SD	19.4 ± 5.5	19.1 ± 5.6	19.2 ± 6.6	18.6 ± 5.7
Brain natriuretic peptide, mean ± SD	133.2 ± 157.4	155.7 ± 180.4	96.5 ± 125.7	101.6 ± 137.3
Systolic blood pressure, mean ± SD	119.8 ± 17.7	122.7 ± 17.8	121.9 ± 17.3	124.1 ± 16.4
Diastolic blood pressure, mean ± SD	68.7 ± 9.7	70.2 ± 9.6	71.1 ± 10.7	73.1 ± 10.1*
Distance walk (meters), mean ± SD	346.4 ± 104.6	335.7 ± 101.0	370.7 ± 106.6	377.8 ± 104.0
LVEF calc (%), mean ± SD	28.5 ± 3.0	28.7 ± 3.4	28.7 ± 3.7	28.9 ± 3.4
LVEDV indexed by BSA (ml/m ²), mean ± SD	123.0 ± 26.5	125.0 ± 27.6	129.9 ± 34.7	125.3 ± 29.0
LVESV indexed by BSA (ml/m ²), mean ± SD	88.2 ± 20.5	89.5 ± 22.7	93.4 ± 28.6	89.6 ± 23.5
GFR (ml/min/1.73 m ²), mean ± SD	48.4 ± 8.2	48.0 ± 8.5	79.0 ± 15.8	79.9 ± 16.1

ICD, implantable cardioverter-defibrillator; CRT-D, cardiac resynchronization therapy with defibrillator; NYHA, New York Heart Association; CHF, congestive heart failure; CABG, coronary artery bypass graft; ACE, inhibitor angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; LVEF, left ventricular ejection fraction; BSA, body-surface area.

*p-value < .05 referring to comparison of ICD to CRT-D within a given GFR group.

^aThe body mass index is the weight in kilograms divided by the square of the height in meters.

death ($p = .02$). Similarly, among patients with $45 < \text{GFR} < 60$, CRT-D was associated with a lower probability of any VT/VF/death ($p = .074$) using the Kaplan-Meier method. Multivariable analysis revealed that CRT-D was associated with a 30% reduction in risk of any VT/VF/death ($p = .14$).

2.3 | Effect of chronic kidney disease on cardiac reverse remodeling associated with CRT-D

In CRT-D patients with LBBB, there was no significant difference in the average percent reduction in LVESV ($p = .989$), LVEDV ($p = .859$), and LAV ($p = .930$) 1 year after CRT-D implantation by the presence

of CKD at baseline (Fig. 3), suggesting that the reduction in VT/VF events was independent of LV or LA reverse remodeling.

2.4 | Sensitivity analyses

We performed a number of sensitivity analyses to assess the robustness of our findings. Additional multivariable analyses with adjustments for past atrial arrhythmias and medications including antiarrhythmic drugs and diuretics were performed, revealing similar findings (data not shown). We investigated the effect of BUN alone, creatinine alone, and BUN/creatinine ratio on VTAs, and found GFR to be the strongest predictor of outcomes. We evaluated the effects

FIGURE 1 Kaplan-Meier estimates of the cumulative probability of any VT/VF/death in patients with CKD (A) and without CKD (B) for LBBB patients by CRT-D versus ICD only

of GFR as a continuous variable using a log scale, showing consistent results. However, for easier interpretation, findings are reported based on GFR categories.

3 | DISCUSSION

This study demonstrates that, among mild HF patients with LBBB, CRT-D is associated with reduced risk of VTAs regardless of the presence of CKD at baseline, and this effect is independent of CRT-induced left ventricular reverse remodeling.

CRT decreases the risk of death and HF events as well as VTAs for patients with depressed LV ejection fraction and prolonged QRS (Arya et al., 2005; Barsheshet et al., 2011; Cleland et al., 2005; Di Biase et al., 2008; Ermis et al., 2005; Linde et al., 2008; Moss et al., 2005, 2009). Given recent studies, there is greater understanding of the impact of renal dysfunction on benefit derived from CRT, but little is known about the effects of baseline renal function on VTAs among patients receiving CRT (Daimee et al., 2015; Goldenberg et al., 2010; Lin et al., 2011; Van Bommel et al., 2011). From MADIT-CRT, prior studies related to renal function have described the association of BUN/Cr ratio and GFR on the outcomes of death and HF events (Daimee et al., 2015; Goldenberg et al., 2010). This study is the first to report the relationship between CKD- and CRT-derived benefit in reducing VTA risk among MADIT-CRT patients.

From extensive research among dialysis patients, end-stage renal disease is known to predispose to the development of VTAs and SCD, risks that may be present in the context of predialysis CKD as well (Bonato et al., 2013; Chakko & Gheorghiade, 1985; Whitman et al., 2012). In our analysis, patients with and without CKD both experienced similar reduction in risk of VTAs after CRT-D implantation. For the end point of any VT/VF, the risk reduction among CKD patients was statistically nonsignificant, although effect size of this reduction

was similar in CKD and non-CKD patients, as evidenced by the hazard ratios (Table 2).

Furthermore, among those with CKD, the association between CRT-D and VTA risk reduction was consistent for patients with GFR ≤ 45 and $45 < \text{GFR} < 60$. It is conceivable that, in our mild HF population, renal dysfunction does not compromise benefit from CRT-D in comparison to advanced HF patients. These findings are particularly relevant as CKD patients were more likely to present with comorbidities such as diabetes, hypertension, and ischemic cardiomyopathy that are associated with VTAs. In our cohort, the presence of ischemic disease among patients with and without CKD was not associated with the risk of VTAs and did not influence benefit from CRT-D in reducing VTA risk in either renal function group. Both cardiac and noncardiac death rates were similar regardless of baseline CKD status.

Patients in both renal function categories also experienced similar echocardiographic improvement with CRT-D, measured as volumetric response 1 year after CRT-D implantation, suggesting that the prognostic significance of CKD is independent of cardiac reverse remodeling. While we can speculate that GFR improvement in CRT-D subjects may have contributed to the lower VTA risk, follow-up GFR data are not available in MADIT-CRT.

Our data suggest that mild HF patients with LBBB, with or without CKD, experience beneficial effects from CRT-D in reducing VTAs. Therefore, the important clinical implication of our study is that CKD patients should still be considered for CRT-D implantation. Additional prospective studies are needed to characterize VTAs in the population of patients with mild symptomatic HF and more significant CKD, particularly by assessing the role of GFR changes in the setting of CRT.

3.1 | Limitations

Our investigation has certain limitations. As stated, MADIT-CRT considered only patients with mild HF and creatinine ≤ 3.0 mg/dl, limiting

FIGURE 2 Kaplan-Meier estimates of the cumulative probability of any VT/VF in patients with CKD (A) and without CKD (B), and fast VT/VF in patients with CKD (C) and without CKD (D) for LBBB patients by CRT-D versus ICD only

TABLE 2 Treatment effect of CRT-D versus ICD only by baseline GFR category on the risk of any VT/VF/death, any VT/VF, and fast VT/VF in patients with an LBBB ECG pattern

Parameter	Hazard ratio	95% CI	p-value	Interaction p-value
End point: Any VT/VF/death (316 events)				
CRT-D: ICD in those with GFR < 60	0.61	0.41–0.89	.010	.630
CRT-D: ICD in those with GFR ≥ 60	0.68	0.52–0.89	.005	
End point: Any VT/VF (243 events)				
CRT-D: ICD in those with GFR < 60	0.68	0.42–1.10	.113	.887
CRT-D: ICD in those with GFR ≥ 60	0.65	0.48–0.88	.005	
End point: Fast VT/VF (153 events)				
CRT-D: ICD in those with GFR < 60	0.49	0.25–0.96	.038	.763
CRT-D: ICD in those with GFR ≥ 60	0.55	0.39–0.80	.001	

The model is adjusted for current smoking, ischemic cardiomyopathy, prior myocardial infarction, systolic blood pressure, weight, and worst New York Heart Association heart failure stage. Furthermore, the models for any VT/VF and fast VT/VF are taking the competing risk of all-cause mortality into consideration using the Fine and Gray competing risk analyses. All interaction p -values between GFR < 60 and GFR ≥ 60 groups were nonsignificant ($p > .10$).

FIGURE 3 Mean percent reduction in left ventricular end-diastolic volume, left ventricular end-systolic volume, and left atrial volume at 1 year after CRT-D implantation by baseline GFR. Abbreviations: LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LAV, left atrial volume

our ability to assess patients with more advanced HF and renal disease. Follow-up renal function data were not collected in MADIT-CRT, and we were thus not able to assess the role of any changes in renal function over time. Our study was a post hoc analysis and includes all the inherent bias of such analyses. We adjusted our models for various relevant covariates; however, unmeasured confounders could not be taken into consideration.

4 | CONCLUSIONS

In this study, mild HF patients with low left ventricular EF and LBBB morphology, both with and without CKD at baseline, experienced a significantly lower risk of VTAs after CRT-D implantation, independent of cardiac reverse remodeling.

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DISCLOSURES

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