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Examination of the Effect of Implantable Cardioverter-Defibrillators on Health-Related Quality of Life:

Based on Results from the Multicenter Automatic Defibrillator Trial-II

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Abstract

Background—While implantable cardioverter-defibrillators (ICDs) improve survival, their benefit in terms of health-related quality of life (HRQOL) is negligible.

Objective—To examine how shocks and congestive heart failure (CHF) mediate the effect of ICDs on HRQOL.

Methods—The US patients from the MADIT-II (Multicenter Automatic Defibrillator Trial-II) trial (n = 983) were randomized to receive an ICD or medical treatment only. HRQOL was assessed using the Health Utility Index 3 at baseline and 3, 12, 24, and 36 months following randomization. Logistic regressions were used to test for the effect of ICDs on the CHF indicator, and linear regressions were used to examine the effect of ICD shocks and CHF on HRQOL in living patients. We used a Monte Carlo simulation and a parametric Weibull distribution survival model to test for the effect of selective attrition. Observations were clustered by patients and robust standard errors (RSEs) were used to control for the non-independence of multiple observations provided by the same patient.

Results—Patients in the ICD arm had 41% higher odds of experiencing CHF since their last assessment compared with those in the control arm (RSE = 0.19, p = 0.01). Developing CHF reduced HRQOL at the subsequent visit by 0.07 (p < 0.01). Having ICD shocks reduced overall HRQOL by 0.04 (p = 0.04) at the subsequent assessment. The negative effect of ICD firing on HRQOL was an order of magnitude greater than the effect of CHF.

Conclusions—A higher prevalence of CHF and shocks among patients with ICDs and their negative effect on HRQOL may partially explain the lack of HRQOL benefit of ICD therapy.

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Andrew Dick and Honhwei Zhao have no conflicts of interest to declare.

Background

As the clinical indications for implantable cardioverter-defibrillators (ICDs) have broadened, utilization rates of ICDs have been rapidly increasing, making ICDs the most common cardiovascular device in contemporary clinical use. In 2005, >40 000 Medicare beneficiaries in the US received an ICD for primary or secondary prevention of sudden cardiac death.[1]

The MADIT-II (Multicenter Automatic Defibrillator Trial-II) study provided strong evidence that ICD therapy extends life but provides little or no quality-of-life (QOL) benefits.[2,3] Considering the health-related QOL (HRQOL) effect of an ICD is important; HRQOL reflects a person's well-being among multiple dimensions of health and incorporates the preferences of a patient for his/her health state.[4–6]

There could be several plausible explanations for the lack of a quality-adjusted life-year (QALY) benefit with ICDs, in contrast with the substantial survival benefit of these devices. First, the ICD may generate psychological problems, with deleterious effects on HRQOL. Studies have demonstrated that 30–50% of ICD recipients experience fear, anxiety, or depression following ICD implantation.[7–9] Both appropriate and inappropriate shocks associated with the ICD may diminish HRQOL by contributing to a patient's anxiety.[10,11] Second, the ICD device may have a negative impact on a person's health. Goldenberg et al.[12] showed that an ICD reduces the risk of sudden death but increases the likelihood of later heart failure events. Based on the general observation that providing care to patients with the worst health is more cost effective compared with care for patients with less severe disease, the survival benefit of an ICD is expected to be greater for those at higher risk of death and those with worse health status.[13] Third, with the help of an ICD, sicker patients are more likely to survive.[3] Hence, over time, this effect would result in a lower average HRQOL among those with an ICD compared with those in the control group (so-called selective attrition), and consequently reduce the magnitude of any ICD effect on QALYs.

Using the data from the MADIT-II trial, the aim of our study was to test the above three explanations, and examine the extent to which shocks and developing congestive heart failure (CHF) associated with an ICD explain the lack of any positive HRQOL effect. Finally, we discuss the impact of our results on clinical practice and policy.

Methods

Clinical Data

Overview of the Trial—The MADIT-II examined the effect of transvenous defibrillator systems (Guidant, St. Paul, MN, USA). Reports detailing the methods and clinical outcomes of the clinical trial,[3] ICD cost per life-year,[14] and HRQOL effects[2] have been published elsewhere.

Patients with a prior myocardial infarction and a left ventricular ejection fraction of ≤0.30 (n = 1232) were randomly assigned to receive either an ICD (n = 742) or conventional medical treatment (CONV) [n = 490]. Patients were systematically followed annually for up to 4

years until trial close-out. The primary outcome of the study was all-cause mortality, with the incidence of adverse events, economic outcomes, and HRQOL effects being secondary outcomes. The trial utilized a rolling enrollment design, with patients being followed up for different periods of time, averaging 20 months. As such, HRQOL data were right censored (at trial termination).

The original HRQOL analysis[2] was based on a subset (n = 1089) of the total trial population as HRQOL questionnaires were not distributed among patients in the European study centers (n = 109) and patients with missing baseline HRQOL data (n = 22) were excluded from the analysis. In addition, patients from study centers with poor data quality (n = 12) were omitted. We demonstrated no differences in QALYs lost for living patients by treatment group (−0.037, p = 0.64) or in overall QALYs lost by treatment group (0.043, p = 0.37) over 3 years.

The current HRQOL analysis was based on a subset (n = 983) of the original HRQOL sample. Patients who had died (n = 25), were censored (n = 35), or had missing data (n = 43) within the first 3 months and patients who experienced an ICD shock before their baseline HRQOL data were collected (n = 3) were excluded from the analysis.

Clinical Events—Data on adverse events, including CHF, were recorded by the physician investigators at 1 month and every 3 months after randomization until close-out. Patients in the ICD study arm underwent quarterly ICD evaluations as well as interim visits if their symptoms dictated.[3] The centers completed ICD follow-up data forms describing each ICD therapy (anti-tachycardia pacing or shock) and downloaded ICD interrogation data to discs.[15] All ICD interrogation data were reviewed by an ICD endpoint committee who adjudicated each ICD-related event. The ICD endpoint committee was blinded to the results of the electrophysiology study results.

Health-Related Quality of Life (HRQOL) Assessment—The HRQOL of each study participant was measured using the Health Utility Index 3 (HUI3)[16] at baseline, and at 3, 12, 24, and 36 months after randomization; any questionnaires returned after trial termination were excluded (n = 8). The HUI3 is a questionnaire that uses a set of health preferences from a healthy population to assess HRQOL across eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain and discomfort. Values can range between −0.371 and 1, with −0.371 being the worst possible health state, 0 being death, and 1 being the best possible health state.[2]

The HUI3 was self-administered during face-to-face study visits, although patients who did not complete the HRQOL assessment during the visit were allowed to complete it at home and return it to the office before the next scheduled visit. Mean HUI3 scores in the CONV arm increased over time from 0.646 to 0.678, while in the treatment arm, they declined (from 0.637 to 0.601).[2] The between-group difference in the mean change in HUI3 score from baseline to the end of each year was significant at year 2 ($p < 0.05$) and marginally significant at year 3 ($p < 0.1$).

Data Analysis

Imputation of Missing HRQOL Data—In the original HRQOL study,[2] missing HRQOL data (8% of observations) were imputed using a multivariate fixed-effects model, regressing the change in HRQOL score from baseline using time, treatment, death during the trial, death within 6 months after the HRQOL assessment, sudden death within 6 months of the HRQOL assessment, presence of diabetes mellitus, use of diuretics, and having New York Heart Association class II–IV heart failure. Each variable was interacted with time, and death indicators were interacted with both time and treatment. Subject-level fixed effects were included to capture the idiosyncratic component of the HUI3 responses of each patient. The missing data were imputed by calculating predicted values using the above model and the estimated individual idiosyncratic component of HRQOL. The HRQOL data were assumed to be missing at random (MAR), conditional on observed patient characteristics and the individual idiosyncratic component, similar to other studies.[17,18]

Monthly HRQOL scores were estimated using linear interpolation between observed values (0, 3, 12, 24, and 36 months). The HRQOL score from the last observation was carried forward to the time of censoring or death, and set to missing thereafter. The change in HRQOL score from baseline at each point was calculated for each patient, and mean profiles were generated for each study arm. For deceased patients, monthly HRQOL scores were estimated using linear interpolation between the last assessment and the time of death, with HRQOL set to zero from that time forward until the end of the study time for that patient.

The same imputed values from the original HRQOL study[2] were used in the current study and, except where noted, all further analyses used the final dataset that included the imputed missing HRQOL values. We used STATA/SE Version 8.2 software (StataCorp LP, College Station, TX, USA) for the modeling and SAS Version 8 for Windows (The SAS Institute, Cary, NC, USA) for data manipulations.

Analyses—The purpose of these analyses was to determine whether shocks associated with the ICD or CHF are associated with the lack of any significant HRQOL benefit with ICD therapy. We considered three possible explanations for the attenuation of an HRQOL effect, as previously mentioned in the Background section: (i) a higher likelihood of CHF in patients with an ICD and a negative impact of CHF on HRQOL; (ii) a negative impact of the ICD on HRQOL; and (iii) selective attrition.

Tests of the first two explanations were based on results from a logistic regression of indicators for CHF, ICD, and other control variables, as well as two linear regressions of HRQOL in living patients on indicators for CHF and ICD, and other control variables. The first linear regression included ICD treatment, and the second included ICD treatment as well as the two clinical variables CHF since the last assessment and ICD shock since the last assessment. Observations were clustered by individual patients and robust standard errors were used to control for non-independence of observations provided by the same patient.

If ICD recipients are more likely to develop CHF, and CHF negatively impacts HRQOL, then the coefficient for ICD in the logistic regression of CHF should be positive, and the coefficient for CHF in the regression of HRQOL should be negative. If shocks among the

ICD recipients generate a lower HRQOL, then the coefficient for the indicator of shock should be negative in the regression of HRQOL. The t statistics from Wald tests were used to test the coefficients.

Furthermore, we estimated the magnitude of the ICD effects through the pathways of CHF and shock based on the QOL equation (see equation 1):

$$\mathrm{HRQQL}=\alpha_0+\alpha_1 \bullet \mathrm{CHF}+\alpha_2 \bullet \mathrm{Shock}+\alpha_3 \bullet \mathrm{ICD}+\alpha_4 \bullet \mathrm{Z} \quad \text{(Eq. 1)}$$

where Z represents the vector of co-variates, with α_1 through α_4 being regression coefficients. The effect of ICD therapy on HRQOL given co-variates Z, which we denote as Δ_Z, is defined as the difference between the expected (E) HRQOL when an ICD is present and absent (see equation 2):

$$\Delta_Z=\mathrm{E}(\mathrm{HRQQL}|\mathrm{ICD}=1,\mathrm{Z})-\mathrm{E}(\mathrm{HRQQL}|\mathrm{ICD}=0,\mathrm{Z}) \quad \text{(Eq. 2)}$$

Expanding these conditional expectations with respect to CHF and shock gives the effect, conditional on the co-variates Z, through the CHF and shock pathways (see equation 3):

$$\Delta_Z=\underbrace{\alpha_1 \bullet (\mathrm{P}(\mathrm{CHF}=1|\mathrm{ICD}=1,\mathrm{Z})-\mathrm{P}(\mathrm{CHF}=1|\mathrm{ICD}=0,\mathrm{Z}))}_{\text{Effect through CHF}}+\underbrace{\alpha_2 \bullet \mathrm{P}(\mathrm{Shock}=1|\mathrm{ICD}=1,\mathrm{Z})}_{\text{Effect through Shock}}+\underbrace{\alpha_3}_{\text{Direct effect}} \quad \text{(Eq. 3)}$$

where the probabilities (P) were estimated based on logistic regressions. Note that the term P(Shock = 1|ICD = 1,Z) can be expanded with respect to any proper partition; for example, it can be expressed as [P(Shock = 1|CHF = 1, ICD = 1,Z)• P(CHF = 1|ICD = 1,Z) + P(Shock = 1|CHF = 0, ICD = 1,Z)• P(CHF = 0|ICD = 1,Z)], which makes it clear that this term captures the full relationship of ICD with shock including a component through CHF. Denoting the effect through CHF as $\Delta_{C,Z}$ and the effect through shock as $\Delta_{S,Z}$ yields the following (see equation 4):

$$\Delta_Z=\Delta_{C,Z}+\Delta_{S,Z}+\alpha_3 \quad \text{(Eq. 4)}$$

We estimated the unconditional effects of ICD through CHF and shocks, denoted Δ_C and Δ_S, respectively, using the total 983 patients as a standardized population to integrate out the co-variates as follows (equation 5):

$$\Delta_C=\frac{1}{983} \bullet \sum_{n=1}^{983} \Delta_{C,Z,n} \text{ and } \Delta_S=\frac{1}{983} \bullet \sum_{n=1}^{983} \Delta_{S,Z,n} \quad \text{(Eq. 5)}$$

where the subscript n indicates the nth observation's contribution. We estimated 95% confidence intervals around the effects using bootstrapped samples (n = 1000) of the study patients.

We used two different approaches to test the hypothesis of selective attrition as a reason for the lack of HRQOL benefit of ICD therapy. One approach was a Monte Carlo simulation of

the sum of differences in the mean QOL scores between the ICD and CONV groups across time points to when a person drops out of the study, and calculating the p-value associated with the observed difference. The other approach was based on a parametric Weibull distribution survival model in which survival is a function of baseline HRQOL interacted with the treatment group indicator; the coefficient for the interaction indicated that survival is differentially associated with baseline HRQOL across the treatment group.

Results

Study Population

Table I summarizes the baseline characteristics of the study population by treatment arm. The only statistically significant difference between the ICD (n = 601) and control (n = 382) groups at baseline was a greater percentage of patients using diuretic therapy in the control group (p= 0.042). The study population was mainly comprised of older adults, with 54% of patients being aged ≥65 years at baseline, and was overwhelmingly male (84%). A number of baseline health indicators suggested that the study population was severely ill (table I). Baseline HUI3 scores averaged 0.644, ranging from −0.25 to 1 with a standard deviation of 0.290.

Effects of Implantable Cardioverter-Defibrillator Therapy on HRQOL

The effect estimate of ICD therapy in the HRQOL model reported in table II was not significant. Regarding the explanation that an ICD has a negative effect on HRQOL because it increases the incidence of debilitating CHF, we found that patients in the ICD arm had 41% higher odds of experiencing CHF since their last assessment compared with those in the CONV arm (p = 0.01; table III), after adjusting for patient characteristics, prior medical history, and time trends. Moreover, our results demonstrated that developing CHF significantly reduced HRQOL by 0.07 points (p < 0.01; table IV), after controlling for the effects of other co-variates. However, having an ICD device did not have a direct significant effect on HRQOL, after controlling for CHF and shocks.

Regarding the explanation that an ICD could negatively impact HRQOL through generating HRQOL-reducing shocks, we found that having shocks independently reduced overall HRQOL at the subsequent assessment by 0.04 points (p = 0.04, table IV).

The estimated effect of an ICD on HRQOL through the CHF pathway was −0.0029 (95% CI −0.0059, −0.0007), and the estimated effect of an ICD on HRQOL through shocks was −0.0235 (95% CI −0.0443, −0.0024). These results showed significant negative estimated effects of ICD therapy on HRQOL through both shocks and CHF. However, the effect of shock was an order of magnitude greater than that of CHF.

Selective Attrition—For testing the hypothesis that selective attrition could be the reason for the lack of detectable HRQOL benefit in our study, neither the Monte Carlo test of the accumulated difference in mean baseline HRQOL scores (p = 0.230) nor the Weibull-based test (p = 0.374) were significant.

Discussion

Previous results from the MADIT-II study demonstrated that while ICD therapy extended life by providing on average an extra 0.167 discounted life-years to the ICD patients within 3.5 years of follow-up, it provided little or no QOL benefits.[2,14] In the study presented here, we tested several plausible explanations for the lack of HRQOL and, consequently, QALY benefit of ICDs in contrast with the significant survival benefit (2 months over a 3.5-year follow-up period[3]). We concluded that the negative effect of ICD shocks and CHF on HRQOL could be responsible for the lack of HRQOL benefit of ICD therapy despite the demonstrated improvement in survival.

First, we demonstrated that developing CHF is associated with having an ICD. In our study, patients in the ICD arm had 41% higher odds of developing CHF within 1 year. This supports earlier observations provided by Goldenberg et al.,[12] who showed that ICDs reduce the risk of sudden death but increase the likelihood of subsequent heart failure events. Moreover, our results demonstrated that developing CHF since the last assessment was significantly associated with lower HRQOL at the subsequent visit, while having the ICD device was not directly significant. Taken together, the higher prevalence of CHF among patients with ICDs and its negative effect on HRQOL may partially explain the lack of HRQOL benefit of ICD therapy in the presence of a non-trivial gain in survival.

Next, we examined the evidence to determine whether the shocks associated with an ICD may have deleterious effects on HRQOL, possibly by causing psychological problems. Our analysis demonstrated a negative relationship between having an ICD fire and subsequent HRQOL. The estimated effect of ICD through shock was an order of magnitude larger than the estimated effect through CHF. This suggests that QOL assessments are much more sensitive to patients experiencing ICD shocks than to the increase in CHF events. Other studies have also demonstrated that both appropriate and inappropriate ICD shocks may diminish HRQOL by contributing to a patient's anxiety[10,11] and that nearly one-half of ICD recipients experience fear, anxiety, or depression following ICD implantation.[7–9]

Another possible explanation for the lack of a HRQOL benefit associated with ICDs over time is selection effects that may be present separately from any negative impacts related to the ICD itself. If selection, or differential censoring through death, explains the observation of no significant difference in mean HRQOL scores between the ICD and CONV groups, then we would have observed patients with lower HRQOL dropping out (by death or censoring) from the CONV group more rapidly than from the ICD group. This implies that as individuals drop out of the sample, the mean baseline HRQOL score of the CONV group would increase relative to the mean baseline HRQOL score of the treatment group. Because our tests of this hypothesis (based on Monte Carlo simulation or the Weibull approach) were not significant, we cannot rule out that the observed non-significant difference was the result of chance. Moreover, we do not consider our study to be sufficiently powered to interpret the lack of significance as indicative of a trivial effect. Therefore, we can not conclude whether selective attrition took place here and, if it did, how much it diminished the ICD benefit in terms of HRQOL.

Our assumption that missing HRQOL data were MAR, conditional on observed patient characteristics and the individual idiosyncratic component, is potentially another limitation of this study. However, as we discussed in a previous paper,[17] selection bias due to patient drop out could potentially go either way, e.g. healthier patients may leave the study because they feel they do not need any more treatment and are too busy with their lives, whereas sicker patients may stop showing up for follow-up appointments because they do not feel well or are too busy taking care of more acute health problems. Since we do not have any data to distinguish the two, we made a neutral decision and assumed MAR.

Finally, the lack of a significant observed ICD effect on HRQOL could result from the limitations of the HUI3 tool. The HUI3 assessment relies on the preferences of the Canadian general population, which could be different from the preferences of elderly patients with heart disease who participated in the MADIT-II study. Based on the MADIT-II study, the mean HRQOL for CHF patients eligible for ICD therapy was low (e.g. the baseline average was 0.64, with 1.0 reflecting perfect health), with HRQOL further declining over time. If patients adapt to disability, adjusting their activities to an evolving realm of possibility, then instruments such as the HUI3 may overestimate the decrease in QOL.[19,20] By contrast, the SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial)[21] used time trade-off assessment of HRQOL and reported an average baseline utility of 0.85 and assumed that HRQOL remained unchanged over time. In addition, if the data on ICD shocks and HRQOL in MADIT-II were non-randomly missing (e.g. missing observations belonged to more sick patients with a greater effect of an ICD on HRQOL), this could potentially explain the observed HRQOL differential over time as well.

Conclusions

The evidence provided here indicates that in addition to health benefits, the use of an ICD may have negative health consequences for some patients, such as an increased risk of CHF. Hence, careful monitoring of ICD patients with respect to new CHF symptoms is needed as well as more research to understand the mechanism of the ICD-CHF causal relationship. Moreover, we also provide evidence that ICD shocks are associated with lower HRQOL. Further studies should explore whether this effect is long-lasting and examine the approaches, both technical and psychological, for minimizing the effect of shocks on patient well-being.

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Table I

Characteristics of the study population[a]

Characteristic	ICD group (n = 601)	Control group (n = 382)
Mean values		
Baseline HUI3 score	0.64	0.65
Baseline SF-12 physical component score	36.20	36.67
Baseline SF-12 mental component score	50.55	50.68
Age at baseline (y)	64.6	64.7
Number of CHF events during the study [range]	0.81 [0–10]	0.65* [0–11]
Number of ICD shocks during the study [range]	3.08 [0–124]	NA
Number of patients (%)		
Male sex	83.0	85.6
Diabetes mellitus	32.8	37.2
NYHA functional class[b] at baseline		
I	35.9	40.6
II	33.8	32.7
III–IV	30.3	26.8
Current or former smoker	80.5	82.2
Coronary bypass surgery, before baseline	58.7	58.4
Interval of >6 mo between most recent myocardial infarction and enrollment	9.6	12.3
Blood nitrogen urine >25 mg/dL at baseline	29.0	30.9
QRS interval ≥0.12 seconds at baseline	50.9	52.6
Hospitalized at baseline	15.0	11.0**
Patients who developed CHF during the study	36.4	34.0
Patients who experienced ICD shocks during the study	32.1	NA
Diuretic use at baseline	73.0	78.8***

[a] All p-values are >0.10 unless otherwise indicated.

[b] Values reflect the highest NYHA functional class recorded in the 3-month period before enrollment. Eligibility was limited to patients who were in NYHA class I, II, or III at the time of enrollment.

CHF = congestive heart failure; **HUI3** = Health Utility Index 3; **ICD** = implantable cardioverter-defibrillator; **NA** = not applicable; **NYHA** = New York Heart Association; **QRS** = duration of QRS complex; **SF-12** = 12-item Short Form Health Survey;

* p = 0.04;

** p = 0.042;

*** p = 0.075.

Table II

Linear regression results: direct effect of an implantable cardioverter-defibrillator (ICD) on health-related quality of life (HRQOL). There were 983 patients who provided 2214 observations

Characteristic	HRQOL while alive		
	effect size	RSE	p-value
ICD arm	**−0.013**	**0.013**	**0.322**
Baseline HUI3 score	0.634	0.028	0.000
Time: 12 mo assessment	−0.019	0.008	0.023
Time: 24 mo assessment	−0.045	0.013	0.001
Time: 36 mo assessment	−0.051	0.020	0.012
Age (y)	−0.001	0.001	0.144
Male sex	0.010	0.020	0.617
Diabetes mellitus	−0.023	0.016	0.148
Diuretic use	−0.021	0.016	0.184
LVEF (%)	−0.002	0.001	0.071
Blood urea nitrogen (mg/dL)	0.000	0.001	0.986
Body mass index	−0.002	0.001	0.144
NYHA classes III–IV	−0.040	0.018	0.025
Atrial fibrillation	−0.027	0.015	0.070
Coronary bypass surgery	0.013	0.014	0.336
eGFR <35 mL/min	−0.024	0.036	0.500
Hospitalized at randomization	0.002	0.024	0.943
No. of prior hospitalizations	−0.005	0.007	0.441
QRS ≥120 ms	−0.027	0.014	0.064
Intercept	0.472	0.077	0.000

eGFR = estimated glomerular filtration rate; **HUI3** = Health Utility Index 3; **LVEF** = left ventricular ejection fraction; **NYHA** = New York Heart Association; **QRS** = duration of QRS complex; **RSE** = robust standard error.

Table III

Logistic regression results: implantable cardioverter-defibrillator (IDC)-associated congestive heart failure (CHF) since the last health-related quality of life assessment. There were 983 patients who provided 2323 observations

Characteristic	Odds ratio[a]	RSE	p-Value
ICD arm	**1.41**	**0.19**	**0.01**
Baseline HUI3 score	0.41	0.09	<0.01
Time: 12 mo assessment	2.00	0.26	<0.01
Time: 24 mo assessment	1.94	0.30	<0.01
Time: 36 mo assessment	2.18	0.51	<0.01
Age (y)	1.00	0.01	0.57
Male sex	0.89	0.15	0.47
Diabetes mellitus	1.26	0.18	0.09
Diuretic use	2.63	0.55	<0.01
LVEF (%)	1.04	0.01	<0.01
Blood urea nitrogen (mg/dL)	1.01	0.01	0.28
Body mass index	1.02	0.01	0.14
NYHA classes III–IV	1.38	0.19	0.02
Atrial fibrillation	1.29	0.18	0.07
Coronary bypass surgery	1.11	0.15	0.43
eGFR <35 mL/min	1.44	0.47	0.27
Hospitalized at randomization	0.90	0.16	0.53
No. of prior hospitalizations	1.14	0.06	0.02
QRS ≥120 ms	1.57	0.21	<0.01

[a] Odds ratio = p/(1−p) where p is the probability of having CHF since the last visit.

eGFR = estimated glomerular filtration rate; **HUI3** = Health Utility Index 3; **LVEF** = left ventricular ejection fraction; **NYHA** = New York Heart Association; **QRS** = duration of QRS complex; **RSE** = robust standard error.

Table IV

Linear regression results: health-related quality of life (HRQOL) adjusted for clinical events. There were 983 patients who provided 2214 observations

Characteristic	HRQOL while alive		
	effect size	RSE	p-value
ICD arm	**−0.005**	**0.014**	**0.740**
CHF since the last assessment	**−0.070**	**0.017**	**0.000**
ICD shock since the last assessment	**−0.044**	**0.021**	**0.037**
Baseline HUI3 score	0.626	0.028	0.000
Time: 12 mo assessment	−0.013	0.009	0.131
Time: 24 mo assessment	−0.039	0.013	0.003
Time: 36 mo assessment	−0.045	0.021	0.029
Age (y)	−0.001	0.001	0.132
Male sex	0.011	0.020	0.590
Diabetes mellitus	−0.021	0.016	0.182
Diuretic use	−0.014	0.016	0.359
LVEF (%)	−0.002	0.001	0.102
Blood urea nitrogen (mg/dL)	0.000	0.001	0.932
Body mass index	−0.002	0.001	0.179
NYHA classes III–IV	−0.037	0.017	0.036
Atrial fibrillation	−0.024	0.014	0.097
Coronary bypass surgery	0.012	0.013	0.358
eGFR <35 mL/min	−0.019	0.036	0.593
Hospitalized at randomization	0.001	0.024	0.956
No. of prior hospitalizations	−0.003	0.007	0.604
QRS ≥120 ms	−0.022	0.014	0.120
Intercept	0.460	0.075	0.000

CHF = congestive heart failure; **eGFR** = estimated glomerular filtration rate; **HUI3** = Health Utility Index 3; **ICD** = implantable cardioverter-defibrillator; **LVEF** = left ventricular ejection fraction; **NYHA** = New York Heart Association; **QRS** = duration of QRS complex; **RSE** = robust standard error.