JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 64, NO. 3, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.01.085

Predictors of an Inadequate Defibrillation Safety Margin at ICD Implantation

Insights From the National Cardiovascular Data Registry

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ABSTRACT

BACKGROUND Defibrillation testing is often performed to establish effective arrhythmia termination, but predictors and consequences of an inadequate defibrillation safety margin (DSM) remain largely unknown.

OBJECTIVES The aims of this study were to develop a simple risk score predictive of an inadequate DSM at implantable cardioverter-defibrillator (ICD) implantation and to examine the association of an inadequate DSM with adverse events.

METHODS A total of 132,477 ICD Registry implantations between 2010 and 2012 were analyzed. Using logistic regression models, factors most predictive of an inadequate DSM (defined as the lowest successful energy tested <10 J from maximal device output) were identified, and the association of an inadequate DSM with adverse events was evaluated.

RESULTS Inadequate DSMs occurred in 12,397 patients (9.4%). A simple risk score composed of 8 easily identifiable variables characterized patients at high and low risk for an inadequate DSM, including (with assigned points) age <70 years (1 point); male sex (1 point); race: black (4 points), Hispanic (2 points), or other (1 point); New York Heart Association functional class III (1 point) or IV (3 points); no ischemic heart disease (2 points); renal dialysis (3 points); secondary prevention indication (1 point); and ICD type: single-chamber (2 points) or biventricular (1 point) device. An inadequate DSM was associated with greater odds of complications (odds ratio: 1.22; 95% confidence interval: 1.09 to 1.37; $p = 0.0006$), hospital stay >3 days (odds ratio: 1.24; 95% confidence interval: 1.19 to 1.30; $p < 0.0001$), and in-hospital mortality (odds ratio: 1.96; 95% confidence interval: 1.63 to 2.36; $p < 0.0001$).

CONCLUSIONS A simple risk score identified ICD recipients at risk for an inadequate DSM. An inadequate DSM was associated with an increased risk for in-hospital adverse events. (J Am Coll Cardiol 2014;64:256–64) © 2014 by the American College of Cardiology Foundation.

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Manuscript received October 7, 2013; revised manuscript received January 22, 2014, accepted January 27, 2014.

Defibrillation testing is often performed at the time of implantable cardioverter-defibrillator (ICD) implantation by purposefully inducing ventricular fibrillation (VF) to establish effective arrhythmia detection and termination. In clinical practice, true defibrillation threshold (DFT) testing, implying repeated VF induction while decrementing shock strength for defibrillation until failure, is rarely performed. Instead, many operators opt to demonstrate termination of VF at least once by a shock energy >10 J below the device's maximal programmable output (1). This defibrillation safety margin (DSM) test specifies the lowest energy tested that was successful instead of the true DFT, and often the device is then programmed to at least 10 J above this value (2). Despite technological advancements, including higher output devices and biphasic waveforms, an inadequate traditional 10-J safety margin for defibrillation may still occur. When an inadequate DSM is encountered, further procedural steps often are required, including changing the characteristics of the discharged energy, repositioning the right ventricular defibrillation lead, or placing a subcutaneous system (3). Therefore, a simple risk score to differentiate ICD recipients at risk for an inadequate DSM would aid implanting physicians with pre-procedural planning and counseling of patients. Moreover, the presence of an inadequate DSM often leads to additional further inductions of VF and repeated defibrillation to test system revisions.

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We analyzed data from the ICD Registry of the National Cardiovascular Data Registry (NCDR), a national registry of ICD implantations that captures detailed clinical, patient, and hospital information as well as in-hospital outcomes. By assessing a large population of ICD recipients, we sought to examine variables available pre-procedurally to develop a simple risk score characterizing patients at risk for an inadequate DSM during DFT testing. We also sought to examine the association between an inadequate DSM and adverse events, including procedural complications, prolonged hospital stays, and in-hospital mortality.

METHODS

DATA SOURCE. The NCDR ICD Registry was created in 2006 to meet the requirements of the Centers for Medicare and Medicaid Services' coverage with evidence development decision (4). The Heart Rhythm Society and American College of Cardiology collaborated to establish the national registry, funded by hospital fees and grants from payers and device companies. Hospitals are mandated to provide data on Medicare beneficiaries receiving ICDs for the primary prevention of sudden cardiac death; however, 71.5% of the 1,375 participating hospitals provide data on all patients undergoing ICD implantation, and these hospitals submit 88.4% of all ICD implantations included in the registry (4). This study included all eligible patients enrolled after the April 2010 implementation of version 2.0 of the ICD Registry, which included defibrillation testing data. ICD Registry data have undergone quality standard testing, including an auditing program to confirm completeness and verify accuracy, as previously detailed (4,5).

STUDY POPULATION. All patients with implantation data submitted to the registry between April 1, 2010, and June 30, 2012, were considered for analysis (n = 337,547). Patients undergoing generator replacement or lead revision only procedures (n = 144,665), those already implanted with a previous ICD or cardiac resynchronization therapy with defibrillator device (n = 143), those in whom DFT testing was not performed (n = 59,778), and those with unknown DFT testing status during the implantation procedure (n = 484) were excluded from the analysis, leaving 132,477 patients from 1,457 facilities.

DEFINITION OF AN INADEQUATE DSM. Patients were categorized as having either an adequate or an inadequate DSM, as defined by the lowest successful defibrillation energy tested during the ICD implantation procedure. An inadequate DSM was defined when the difference between the lowest energy tested that was successful and the maximal output of the device implanted was <10 J. Because our goal was to identify patients in whom a standard right ventricular defibrillation lead by itself did not provide adequate defibrillation, patients with separate high-voltage leads implanted in the superior vena cava or subclavian position (n = 283) or arrays placed subcutaneously (n = 82) also were categorized as having inadequate DSMs, even if the final lowest defibrillating energy was adequate. ICD recipients with upper limit of vulnerability testing during the index ICD procedure were not specifically excluded from the analysis, provided that DFT testing also was performed.

CANDIDATE VARIABLES. We examined 28 variables included in registry-captured data that would be suitable for a risk model as plausibly associated with an inadequate DSM (Table 1). Variables included patient demographics, comorbidities, diagnostic data, and device and lead characteristics.

ABBREVIATIONS AND ACRONYMS

DFT = defibrillation threshold

DSM = defibrillation safety margin

ICD = implantable cardioverter-defibrillator

LVEF = left ventricular ejection fraction

NCDR = National Cardiovascular Data Registry

NYHA = New York Heart Association

VF = ventricular fibrillation

TABLE 1 Baseline Characteristics

Characteristic	Total (n = 132,477)	Adequate DSM (n = 120,080)	Inadequate DSM (n = 12,397)	p Value
Patient demographic characteristics				
Age ≥70 yrs	53,973 (40.7)	49,745 (41.4)	4,228 (34.1)	<0.0001
Male	94,677 (71.5)	85,638 (71.3)	9,039 (72.9)	0.0002
Race				<0.0001
White	102,869 (77.7)	94,374 (78.6)	8,495 (68.5)	
Black	19,294 (14.6)	16,498 (13.7)	2,796 (22.6)	
Hispanic	7,331 (5.5)	6,517 (5.4)	814 (6.6)	
Other	2,983 (2.3)	2,691 (2.2)	292 (2.4)	
Comorbidities				
Congestive heart failure	103,147 (77.9)	93,120 (77.5)	10,027 (80.9)	<0.0001
NYHA functional class				<0.0001
I	19,905 (15.0)	18,246 (15.2)	1,659 (13.4)	
II	46,791 (35.3)	42,768 (35.6)	4,023 (32.5)	
III	61,817 (46.7)	55,597 (46.3)	6,220 (50.2)	
IV	3,451 (2.6)	2,996 (2.5)	455 (3.7)	
Nonischemic dilated cardiomyopathy	46,818 (35.3)	41,548 (34.6)	5,270 (42.5)	<0.0001
Syncope	23,063 (17.4)	21,030 (17.5)	2,033 (16.4)	0.0072
Atrial fibrillation/atrial flutter	35,335 (26.7)	32,016 (26.7)	3,319 (26.8)	0.9622
Ventricular tachycardia	41,262 (31.1)	37,359 (31.1)	3,903 (31.5)	0.6342
Cardiac arrest	14,296 (10.8)	12,903 (10.7)	1,393 (11.2)	0.2399
Ischemic heart disease	79,166 (59.8)	72,679 (60.5)	6,487 (52.3)	<0.0001
Previous myocardial infarction	65,312 (49.3)	60,096 (50.0)	5,216 (42.1)	<0.0001
Previous percutaneous coronary intervention	43,936 (33.2)	40,447 (33.7)	3,489 (28.1)	<0.0001
Previous CABG	39,573 (29.9)	36,454 (30.4)	3,119 (25.2)	<0.0001
Primary valvular heart disease	15,257 (11.5)	13,721 (11.4)	1,536 (12.4)	0.0019
Cerebrovascular disease	18,892 (14.3)	17,210 (14.3)	1,682 (13.6)	0.0283
Chronic lung disease	28,336 (21.4)	25,690 (21.4)	2,646 (21.3)	0.4084
Diabetes	50,629 (38.2)	46,080 (38.4)	4,549 (36.7)	0.0010
Sleep apnea	15,929 (12.0)	14,334 (11.9)	1,595 (12.9)	0.0007
Current renal dialysis	3,992 (3.0)	3,375 (2.8)	617 (5.0)	<0.0001
Hypertension	104,818 (79.1)	95,117 (79.2)	9,701 (78.3)	0.0364
Patient diagnostic data				
Body mass index ≥30 kg/m^2	52,546 (39.7)	47,393 (39.5)	5,153 (41.6)	<0.0001
LVEF (%)				<0.0001
≤30	93,654 (70.7)	84,421 (70.3)	9,233 (74.5)	
30 to ≤40	23,360 (17.6)	21,487 (17.9)	1,873 (15.1)	
>40	15,463 (11.7)	14,172 (11.8)	1,291 (10.4)	
QRS duration ≥120 ms	54,248 (40.9)	49,126 (40.9)	5,122 (41.3)	0.3822
Systolic blood pressure <100 mm Hg	6,676 (5.0)	5,950 (5.0)	726 (5.9)	<0.0001
Creatinine level >2.0 mg/dl	9,626 (7.3)	8,465 (7.0)	1,161 (9.4)	<0.0001
Device and lead characteristics				
ICD indication: primary prevention	105,507 (79.6)	95,722 (79.7)	9,785 (78.9)	0.0388
ICD type				<0.0001
Single chamber	29,111 (22.0)	25,887 (21.6)	3,224 (26.0)	
Dual chamber	56,188 (42.4)	51,556 (42.9)	4,632 (37.4)	
CRT-D	46,924 (35.4)	42,408 (35.3)	4,516 (36.4)	
Single-coil defibrillator lead	23,115 (17.4)	21,077 (17.6)	2,038 (16.4)	<0.0001

Values are n (%). Unadjusted pre-procedural characteristics of ICD recipients with and without adequate DSMs during defibrillation testing are listed.

CABG = coronary artery bypass grafting; CRT-D = cardiac resynchronization therapy with defibrillator; DSM = defibrillator safety margin; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

ADVERSE OUTCOMES. The first adverse outcome of interest was the occurrence of any associated in-hospital complication during or after ICD implantation. The second outcome was the duration of hospitalization, from admission to discharge. For analytical purposes, length of hospital stay was dichotomized to >3 or ≤3 days on the basis of the distribution of the cohort (as a clinically meaningful cutoff and on the basis of a previous ICD Registry study [6], as 90% of the cohort had a hospital stay ≤3 days). The third outcome was the occurrence of in-hospital mortality during or after ICD implantation.

STATISTICAL ANALYSIS. Unadjusted differences in baseline characteristics were compared between patients with adequate versus inadequate DSMs using chi-square tests for categorical variables. A p value <0.05 was considered statistically significant.

To identify the variables most strongly associated with an inadequate DSM, the entire cohort was randomly split into 2 equally sized cohorts. The first cohort was used to develop the models (derivation cohort, 66,118 patients among 1,426 hospitals), whereas the second cohort was used to validate the models (validation cohort, 66,359 patients among 1,405 hospitals). To develop a risk model for predicting an inadequate DSM in those with DFT testing performed, we performed multivariate logistic regression with a stepwise selection method (p value for entry = 0.15, p value for retention = 0.05). Categorical cut points for continuous variables were determined both graphically and on the basis of previous ICD Registry data (6,7). We evaluated model discrimination and calibration by both C-statistics and Hosmer-Lemeshow statistics; low chi-square values and high corresponding p values for the Hosmer-Lemeshow statistic suggest acceptable model calibration and fit to the data (8). For the validation analysis, we investigated model performance by evaluating predictive ability, overfitting indexes, C-statistics, and Hosmer-Lemeshow statistics. We excluded multicollinearity by evaluating Pearson correlation coefficients and variance inflation factors.

To identify a simple risk score predictive of an inadequate DSM, each variable of interest was selected on the basis of its relative contribution in the logistic regression model. Of all candidate variables, a larger model of 16 variables met the retention p value of 0.05. These variables were ranked by the Wald chi-square statistic, and variables with the least contribution were excluded from the model until 8 variables that captured >90% of the full multivariate model were left (the ratio of the global chi-square statistic in the reduced compared with the full model was

evaluated) (9). A point system was derived by assigning a numerical value proportional to the associated beta coefficient found in multivariate analysis. The simple arithmetic sum of the point values assigned to each variable was calculated for all patients, which then constituted the risk score for an inadequate DSM during DFT testing. The adequate performance of the risk score in the validation cohort was confirmed.

Next, we developed hierarchical logistic regression models to assess the independent association of an inadequate DSM with each adverse event, by accounting for clustering of patients within hospitals in multivariate models (10). Covariates in the multivariate models assessing adverse events included patient demographics (age, sex, and race), comorbidities (congestive heart failure, New York Heart Association [NYHA] functional class, nonischemic cardiomyopathy, syncope, atrial fibrillation or atrial flutter, ventricular tachycardia, cardiac arrest, ischemic heart disease, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft surgery, primary valvular heart disease, cerebrovascular disease, chronic lung disease, diabetes, sleep apnea, current renal dialysis, and hypertension), diagnostic data (body mass index, left ventricular ejection fraction [LVEF], QRS duration, systolic blood pressure, and creatinine level), and device and lead characteristics (indication for implantation, device type, single- vs. dual-coil defibrillator lead). The prevalence of missing values was <1% for all variables, except LVEF (1.6%), QRS duration (6.6%), and single- versus dual-coil defibrillation lead (12.0%). For categorical variables with yes-or-no responses, missing data were assumed to represent no responses. For variables with >1% missing data, the median value for the entire cohort was imputed, and a dummy variable indicating whether the variable was missing was created. As a secondary analysis, we repeated the model analyses using the multiple imputation method to handle missing values, which produced no meaningful changes of the results. Multiple imputations were performed on the basis of the EM algorithm, as previously described (11). Statistical tests were 2 sided and considered significant if they yielded p values <0.05. Analyses were performed using SAS Statistical Package version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

Of 132,477 total ICD recipients with defibrillation testing performed, inadequate DSMs occurred in 12,397 patients (9.4%). Baseline characteristics of the study population as a whole and the unadjusted association of each characteristic with an adequate versus an inadequate DSM are presented in **Table 1**. In unadjusted analysis, variables associated with an inadequate DSM included younger age, male sex, nonwhite race, congestive heart failure, worsened NYHA heart failure class, nonischemic cardiomyopathy, primary valvular heart disease, sleep apnea, current renal dialysis, higher body mass index, lower LVEF, lower systolic blood pressure, higher creatinine level, secondary prevention indication, single-chamber or cardiac resynchronization therapy defibrillator implantation, and single-coil defibrillator lead implantation. Inadequate DSMs occurred less often in ICD recipients with histories of syncope, ischemic heart disease, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft surgery, cerebrovascular disease, and diabetes. In general, ICD recipients with known status of defibrillation testing included in the study differed from ICD recipients who required exclusion because of unknown status of defibrillation testing with respect to several preprocedural characteristics (Online Table 1).

RISK SCORE FOR AN INADEQUATE DSM. For the derivation cohort, the multivariate stepwise logistic regression for the outcome of an inadequate DSM resulted in a larger model composed of 16 variables, with a C-statistic of 0.603 and a Hosmer-Lemeshow goodness-of-fit chi-square statistic of 5.68 (p = 0.6832). The simple risk score was constructed from 8

TABLE 2 Multivariate Predictors of an Inadequate DSM

Description	Wald Chi-Square	Beta Coefficient	OR	95% CI	Points
Intercept	4,853.4	−3.03			
Age <70 yrs	42.2	0.19	1.21	1.14–1.28	1
Male	38.9	0.19	1.21	1.14–1.29	1
Black race	234.7	0.53	1.70	1.59–1.82	4
Hispanic	20.5	0.25	1.29	1.15–1.44	2
Other nonwhite race	1.5	0.11	1.11	0.94–1.32	1
NYHA class III	43.0	0.20	1.23	1.15–1.30	1
NYHA class IV	43.5	0.49	1.64	1.41–1.89	3
No ischemic heart disease	75.5	0.25	1.28	1.21–1.35	2
Current renal dialysis	63.3	0.50	1.65	1.46–1.86	3
ICD indication: secondary prevention	22.1	0.16	1.17	1.10–1.26	1
ICD type: single chamber	55.8	0.26	1.30	1.21–1.39	2
ICD type: CRT-D	18.9	0.15	1.16	1.09–1.25	1

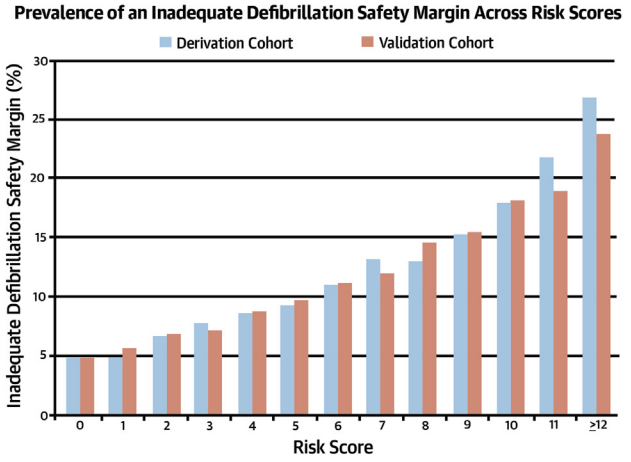
Statistically significant predictors associated with an inadequate DSM after multivariate adjustment in the derivation cohort are listed. Full model C-statistic = 0.597; Hosmer-Lemeshow goodness-of-fit test: chi-square statistic = 5.56, p = 0.6969.

CI = confidence interval; OR = odds ratio; other abbreviations as in **Table 1**.

variables, which accounted for >90% of the explained variance (Table 2). The multivariate model from the same derivation cohort limited to these 8 variables resulted in a C-statistic of 0.597 and a Hosmer-Lemeshow goodness-of-fit chi-square statistic of 5.56 ($p = 0.6969$). In the validation cohort, the same 8-variable multivariate model resulted in a C-statistic of 0.597 and a Hosmer-Lemeshow goodness-of-fit chi-square statistic of 8.49 ($p = 0.3874$). P values >0.05 in all models suggested reasonable calibration, with acceptable model fit to the data. An additional approach for model validation was undertaken to confirm that the predicted prevalence of an inadequate DSM was indeed associated with a higher observed prevalence of an inadequate DSM in the validation cohort (Online Fig. 1).

Predictors (Risk Score Points)

•Age <70	(1 point)
•Male sex	(1 point)
•Race	
Black	(4 points)
Hispanic	(2 points)
Other	(1 point)
•Heart failure class	
New York Heart Association Class III	(1 point)
New York Heart Association Class IV	(3 points)
•No Ischemic heart disease	(2 points)
•Renal dialysis	(3 points)
•Secondary prevention indication	(1 point)
•ICD type	
Single-chamber device	(2 points)
Biventricular device	(1 point)



CENTRAL ILLUSTRATION **Predictors and Risk Score of an Inadequate DSM at Implantable Cardioverter-Defibrillation Implantation**

In addition to displaying the point system delineation for the risk score used in this study, the proportion of patients with inadequate defibrillation safety margins (DSMs) across risk scores is shown.

The risk for an inadequate DSM increased from 4.9% in ICD recipients with scores of 0 (0.8% of the total cohort) to 24.5% in ICD recipients with scores ≥12 (0.5% of the total cohort). Among ICD recipients with risk scores ≤3 (39.6% of the entire cohort), 6.8% experienced inadequate DSMs. In contrast, among ICD recipients with risk scores ≥7 (18.0% of the entire cohort), 14.9% experienced inadequate DSMs. The distribution of the risk score and the percent of patients with inadequate DSMs among different risk score groups in both the derivation and validation cohorts are shown in the Central Illustration and Figure 1.

ASSOCIATION OF AN INADEQUATE DSM WITH PROCEDURE COMPLICATIONS. As shown in Table 3, the crude risk for any associated procedural complication was higher in those with inadequate DSMs (2.69%) than in those with adequate DSMs (2.33%). Both unadjusted and multivariate-adjusted analyses of the association between an inadequate DSM and complications are shown in Figure 2. After adjustment for potential confounders, those with inadequate DSMs had significantly greater odds of any associated procedural complication (odds ratio: 1.22; 95% confidence interval: 1.09 to 1.37; $p = 0.0006$).

ASSOCIATION OF AN INADEQUATE DSM WITH LENGTH OF HOSPITAL STAY. The mean length of hospital stay for the entire cohort was 1.65 ± 3.82 days. The mean length of stay was significantly longer in ICD recipients with inadequate DSMs than in those with adequate DSMs (1.93 ± 4.60 vs. 1.62 ± 3.73, $p < 0.0001$), as seen in Table 3. Both unadjusted and multivariate-adjusted analyses of the association between an inadequate DSM and length of hospital stay are shown in Figure 2. After adjustment for potential confounders, ICD recipients with inadequate DSMs had greater odds of a hospital stay >3 days compared with those with adequate DSMs (odds ratio: 1.24; 95% confidence interval: 1.19 to 1.30; $p < 0.0001$).

ASSOCIATION OF AN INADEQUATE DSM WITH IN-HOSPITAL MORTALITY. The crude risk for in-hospital mortality was significantly higher in those with inadequate DSMs (0.40%) compared with those with adequate DSMs (0.20%) (Table 3). Both unadjusted and multivariate-adjusted analyses of the association between an inadequate DSM and in-hospital mortality are shown in Figure 2. After adjustment for potential confounders, ICD recipients with inadequate DSMs experienced greater odds of in-hospital mortality compared with those with adequate DSMs (odds ratio: 1.96; 95% confidence interval: 1.63 to 2.36; $p < 0.0001$).

DISCUSSION

In a large, nationally representative sample of 132,477 ICD recipients undergoing DFT testing over a 2-year period, approximately 1 in 10 patients (9.4%) failed to have adequate DSMs despite the implantation of modern devices. We identified several patient characteristics that predicted an inadequate DSM and developed a simple risk score using 8 pre-procedural variables to help distinguish those ICD recipients at higher and lower risk. After multivariate adjustment for potential confounders, an inadequate DSM discovered during DFT testing was associated with more than 20% greater odds of other procedural complications and prolonged hospital stay (>3 days) and almost 2-fold greater odds of in-hospital mortality.

Previous studies examining the incidence and predictors of an inadequate DSM were smaller, did not include modern devices with higher maximal output (35 to 41 J), and were not powered to detect differences in complications and other adverse events during and immediately after device implantation (12–15). The prevalence of a high DFT or an inadequate DSM in these previous studies ranged from 3.9% to 11%. Altogether, variables predictive of a high DFT or an inadequate DSM in these studies included worsened NYHA class, low LVEF, no history of bypass surgery, no history of myocardial infarction, prior amiodarone use, VF as the presenting rhythm, QRS duration ≥200 ms, larger left ventricular end-diastolic dimension, and prolonged procedure time. Two of these previous studies evaluated subsequent outcomes in those with abnormal defibrillation testing parameters. Shukla et al. (12) found that a high DFT did not affect 6-month survival in the cohort, while Mainigi et al. (13) found that an elevated DFT itself was not associated with worsened 2-year mortality. In the present study, despite the use of more modern devices with higher maximal energy output, a 9.4% prevalence of an inadequate DSM was similar to previously reported studies, potentially suggesting the implantation of a sicker heart failure patient population with contemporary ICDs. Unfortunately, the ICD Registry used in the present study does not contain comprehensive echocardiographic and pre-procedural medication data, and therefore left ventricular dimension and amiodarone use could not be analyzed in our multivariate models. However, with more than 12,000 events that met the criteria for an inadequate DSM, our study provided ample power to identify a simple risk score that could be used by clinicians to more accurately assess the risk for an inadequate DSM. By distinguishing ICD recipients with lower risk (score ≤3) and higher risk (score ≥7) for an inadequate DSM with variables available before the procedure, the simple risk score may aid operators in preparing for ICD procedures on the basis of the estimated risk for an inadequate DSM occurring during the procedure. It is particularly important to identify ICD recipients with high risk for an inadequate DSM, given the greater likelihood that a change in clinical management may be required. Also, armed with information from the simple risk score, operators may be better able to counsel patients regarding the probability of requiring additional steps to the procedure, including the need for additional hardware and/or testing. Operators also may be better prepared and be able to alter their approaches (such as repositioning or ensuring that the device implanted has programmable energy characteristics that can be altered) in those ICD recipients most vulnerable. It should be noted that ICD recipients with lower risk scores (≤3) still had a measurable 4.8% to 6.8% prevalence of an inadequate DSM during DFT testing, suggesting that the risk score proposed in the present study was still unable to perfectly predict those ICD recipients who were not at risk for an inadequate DSM.

Although our study was not equipped to identify the underlying mechanisms responsible for associations between predictors that constituted the simple risk score and an inadequate DSM and should therefore be considered hypothesis generating, several plausible explanations could be entertained. The

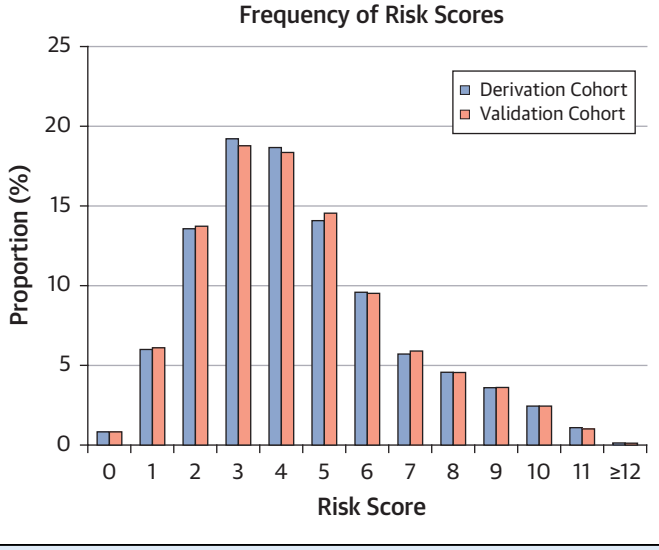


FIGURE 1 Distribution of Risk Scores

The distributions of risk scores for an inadequate defibrillation safety margin (DSM) are shown for both the derivation and validation cohorts.

associations of age <70 years and male sex with an inadequate DSM may be related to more muscle or tissue mass, not fully captured by the body mass index measurement, blunting the effect of defibrillation energy delivered and increasing the chance of an inadequate DSM. Those of nonwhite race had increased risk for an inadequate DSM, which was most prominent in blacks. It is plausible that unmeasured factors may explain this association, including those related to disparities in health care experienced by nonwhite races or the existence of left ventricular hypertrophy (16). An association between worsened NYHA heart failure class and an inadequate DSM has previously been described (15) and may be related to enlarged cardiac chambers or overall end-stage disease that results in an inability to terminate VF even with high-energy shocks. Similarly, a lack of ischemic heart disease may indicate a susceptibility to difficult arrhythmia termination in those with nonischemic cardiomyopathy. Patients currently on renal dialysis may be at risk for an inadequate DSM for a multitude of reasons, including left ventricular hypertrophy (17) or electrolyte abnormalities that may alter cardiac electrical properties (18). A secondary prevention indication for ICD implantation may act as a marker for patients at risk for intractable malignant arrhythmias, a worsened comorbid state, or amiodarone use. The addition of an atrial lead that comprises a dual-chamber ICD device would not be expected to inherently improve the DFT. Therefore, the underlying mechanism of a protective association from dual-chamber ICD implantation remains uncertain and will need to be examined more thoroughly.

TABLE 3 Adverse Events Stratified by Defibrillation Safety Margin Status

Adverse Event	Total (n = 132,477)	Adequate DSM (n = 120,080)	Inadequate DSM (n = 12,397)	p Value
Any complication	3,136 (2.26)	2,802 (2.33)	334 (2.69)	0.0119
Length of stay (implant to discharge), days	1.65 ± 3.82	1.62 ± 3.73	1.93 ± 4.60	<0.0001
In-hospital mortality	292 (0.22)	242 (0.20)	50 (0.40)	<0.0001
Specific associated complication				
Cardiac arrest	217 (0.16)	170 (0.14)	47 (0.38)	0.0000
Cardiac perforation	71 (0.05)	59 (0.05)	12 (0.10)	0.0290
Set screw problem	39 (0.03)	31 (0.03)	8 (0.06)	0.0167
Lead dislodgement	1,241 (0.94)	1,120 (0.93)	121 (0.98)	0.6335
Pneumothorax	430 (0.32)	391 (0.33)	39 (0.31)	0.8372
Hematoma	417 (0.31)	368 (0.31)	49 (0.40)	0.0929
Coronary venous dissection	146 (0.11)	130 (0.11)	16 (0.13)	0.5063
Device-related infection	108 (0.08)	95 (0.08)	13 (0.10)	0.3389
Pericardial tamponade	72 (0.05)	62 (0.05)	10 (0.08)	0.1867
Transient ischemic attack or stroke	66 (0.05)	57 (0.05)	9 (0.07)	0.2326
Drug reaction	55 (0.04)	49 (0.04)	6 (0.05)	0.6928
Venous obstruction	41 (0.03)	35 (0.03)	6 (0.05)	0.2460
Conduction block	40 (0.03)	34 (0.03)	6 (0.05)	0.2204
Hemothorax	31 (0.02)	28 (0.02)	3 (0.02)	0.9513
Myocardial infarction	27 (0.02)	24 (0.02)	3 (0.02)	0.7544
Urgent cardiac surgery	20 (0.02)	19 (0.02)	1 (0.01)	0.5034
Peripheral embolus	17 (0.01)	16 (0.01)	1 (0.01)	0.6227
Peripheral nerve injury	2 (0.00)	2 (0.00)	0 (0.00)	0.6495
Cardiac valve injury	1 (0.00)	1 (0.00)	0 (0.00)	0.7480

Values are n (%) or mean ± SD. Prevalence of adverse events and specific complications from ICD implantation stratified by an adequate versus an inadequate DSM are listed.

Abbreviations as in Table 1.

An inadequate DSM may lead to additional DFT testing that itself can be associated with complications related to shocks or induced VF with concomitant hypoperfusion, potentially leading to significant morbidity and mortality. Refractory VF with failed multiple defibrillations can occur, and pulseless electrical activity has been reported after termination of VF (19). Significantly greater odds of adverse events in those with inadequate DSMs were consistent across all 3 outcomes studied and persisted despite adjustment for potential confounders. These increased risks have important ramifications relevant to patients and practicing physicians, particularly because these events will likely adversely affect patient quality of life and translate into increased health care utilization and costs. Although it is possible that an increased DSM and the additional defibrillations that invariably resulted from the subsequent further DFT testing directly resulted in an increased risk for all 3 adverse outcomes, alternative explanations should be entertained. For example, it is possible that residual confounding by unmeasured factors explains part or all of the association between an inadequate DSM and adverse events. In general, our simple risk score identified may be useful to operators when counseling patients regarding the overall risks versus benefits of ICD implantation. However, this cross-sectional study evaluating in-hospital outcomes underscores the need for long-term outcome data regarding ICD recipients who do and do not undergo DFT testing, in addition to specific data regarding long-term outcomes in those with inadequate DSMs. It is possible that data from the SIMPLE (Shockless Implant Evaluation) trial comparing outcomes in ICD recipients randomized to DFT versus no DFT testing may provide further insights (20).

STUDY LIMITATIONS. First, because of limitations of the data collected in the ICD Registry, we were not able to assess the impact of several covariates previously associated with a high DFT during ICD implantation, including echocardiographic parameters such as left ventricular mass or size, admission medications such as amiodarone, and specific procedural characteristics such as total procedural time (12,14,21). Omission of

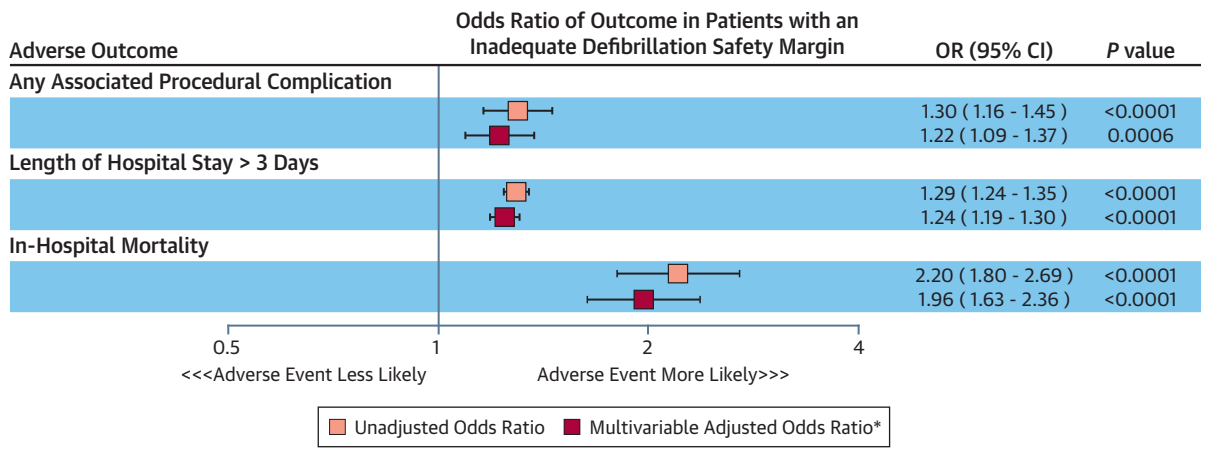


FIGURE 2 Inadequate DSM During ICD Implantation and Adverse Events in ICD Recipients

Unadjusted **(salmon boxes)** and multivariate-adjusted **(red boxes)** odds ratios (ORs) of any associated procedural complication, length of hospital stay >3 days, and in-hospital mortality among implantable cardioverter-defibrillator (ICD) recipients with inadequate defibrillation safety margins (DSMs) during defibrillation testing. The reference group for each analysis is ICD recipients with adequate DSM. The **horizontal error bars** denote 95% confidence intervals (CIs). *Adjusted for patient demographics (age, sex, and race), comorbidities (congestive heart failure, New York Heart Association functional class, nonischemic cardiomyopathy, syncope, atrial fibrillation or atrial flutter, ventricular tachycardia, cardiac arrest, ischemic heart disease, previous myocardial infarction, previous percutaneous coronary intervention, previous coronary artery bypass graft surgery, primary valvular heart disease, cerebrovascular disease, chronic lung disease, diabetes, sleep apnea, current renal dialysis, and hypertension), diagnostic data (body mass index, left ventricular ejection fraction, QRS duration, systolic blood pressure, and creatinine level), and device and lead characteristics (indication for implantation, device type, single- vs. dual-coil defibrillator lead).

these covariates may reduce the utility of the risk score identified in our study, although we were still able to identify 8 variables that differentiated ICD recipients at risk for an inadequate DSM.

Second, although we performed internal validation by using both derivation and validation cohorts from the total ICD Registry population, we did not perform external validation in a different population. Therefore, the risk score may not be generalizable to other ICD populations, such as those in different countries or who did not undergo DFT testing.

Third, the simple risk score did not have ideal discriminative ability in predicting those with adequate versus inadequate DSMs, and we cannot rule out the possibility that unmeasured variables may have provided better discrimination. However, this is the first described risk model that relied on a simply calculated score to aid clinicians in classifying the risk for an inadequate DSM in ICD recipients.

Finally, as with any observational study, we cannot exclude the possibility that residual confounding explains the associations found between an inadequate DSM and other procedural complications, prolonged hospital stays, and in-hospital mortality despite our extensive attempts at multivariate adjustment. For example, although multiple comorbidities were controlled for, because of the possibility of unmeasured confounders, a high DFT and an inadequate DSM may have been markers for ICD recipients who were more ill and, therefore, more likely to experience adverse events.

CONCLUSIONS

In a large, national registry of first-time ICD recipients, specific patient characteristics predicted an inadequate DSM during DFT testing that was captured by a simple risk score to differentiate those at higher and lower risk. An inadequate DSM at the time of ICD implantation was associated with subsequent adverse events, including procedural complications, prolonged hospital stays, and in-hospital mortality. This simple risk score may identify ICD recipients in whom DFT testing is most likely to change clinical management, therefore distinguishing those who most warrant this testing. Future studies are necessary to evaluate the mechanisms underlying the association between an inadequate DSM and adverse events and whether DFT testing itself is responsible for the adverse outcomes observed.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: Nearly 1 in 10 patients have inadequate DSMs during the implantation of ICDs, and this is associated with a higher risk for complications, prolonged hospital stay, and in-hospital mortality.

COMPETENCY IN MEDICAL KNOWLEDGE 2: The following risk factors are associated with an inadequate DSM: age <70 years (1 point); male sex (1 point); black race (4 points), Hispanic ethnicity (2 points), or other non-Caucasian ethnicity (1 point); NYHA functional class III (1 point) or IV (3 points) heart failure; absence of ischemic heart disease (2 points); end-stage renal disease requiring dialysis (3 points); secondary prevention indication (1 point); and single-chamber (2 points) or biventricular (1 point) ICD type.

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: Physicians implanting ICDs should know the risk factors associated with an inadequate DSM.

COMPETENCY IN INTERPERSONAL AND COMMUNICATION SKILLS: Physicians should counsel patients at risk for an inadequate DSM regarding the greater chance that they may require additional testing during the implantation procedure to ensure an adequate margin of safety.

TRANSLATIONAL OUTLOOK 1: Future studies should investigate the mechanisms underlying the association between risk factors and defibrillation threshold.

TRANSLATIONAL OUTLOOK 2: Long-term studies are needed to assess the clinical outcomes of patients with inadequate DSMs after ICD implantation.

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KEY WORDS adverse events, complications, defibrillation safety margin, defibrillation threshold, implantable cardioverter-defibrillator, mortality, national registries, risk score

APPENDIX For a supplemental figure and tables, please see the online version of this article.