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Comparison of outcomes in patients undergoing defibrillation threshold testing at the time of implantable cardioverter-defibrillator implantation *versus* no defibrillation threshold testing

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Abstract

Background: *Inability to perform defibrillation threshold (DFT) testing during implantable cardioverter defibrillator (ICD) implantation due to co-morbidities may influence long-term survival.*

Methods: *Retrospective review at The University of Michigan (1999–2004) identified 55 patients undergoing ICD implantation without DFT testing ("No-DFT group"). A randomly selected sample of patients (n = 57) undergoing standard DFT testing ("DFT group") was compared in terms of appropriate shocks, clinical shock efficacy and all-cause mortality.*

Results: *DFT testing was withheld due to hypotension, atrial fibrillation with inability to exclude left atrial thrombus, left ventricular thrombus, CHF and/or ischemia. The No-DFT group had a similar appropriate shock rate, but lower total survival (69.1%* vs. *91.2%, p = 0.004) than the DFT group. The No-DFT group had a higher incidence of ventricular fibrillation (VF) episodes (9.1%* vs. *3.1%, p = 0.037), and deaths attributable to VF (3 of 17 deaths* vs. *0 of 5 deaths) compared to the DFT group. Multivariate analysis found a trend toward increased risk of death in the No-DFT group (HR 3.18, 95% CI 0.82–12.41, p = 0.095) after adjusting for baseline differences in gender distribution, NYHA class and prior CABG.*

Conclusions: *In summary, overall mortality was higher in the No-DFT group. More deaths attributable to VF occurred in the No-DFT group. Thus, DFT testing should therefore remain the standard of care. Nevertheless, ICD therapy should not be withheld in patients who meet appropriate implant criteria simply on the basis of clinical scenarios that preclude routine DFT testing.* (Cardiol J 2007; 14: 463–469)

Key words: implantable cardioverter-defibrillator, threshold testing, prognosis

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Introduction

Implantable cardioverter-defibrillators (ICDs) are the most effective treatment for those patients who are at high risk for life threatening ventricular arrhythmias. Randomized clinical trials have clearly shown that ICDs are superior to antiarrhythmic drug therapy in survivors of cardiac arrest, and that ICDs provide an additional mortality reduction in both patients with ischemic and non-ischemic cardiomyopathy beyond that provided by optimal medical therapy alone [1–8]. With a steadily increasing elderly population [9] and Medicare databases suggesting an underutilization of ICD therapy [10], it is likely that the number of implants will increase exponentially in coming years. It is believed to be important that defibrillation threshold testing (DFT) is performed at the time of ICD implant to confirm a sufficient programmed shock strength [11–13]. Earlier ICD systems frequently required that the location, type or number of electrodes be altered in order to ensure an adequate defibrillation safety margin. Due to advances in lead technology the requirement for ICD system modifications is less frequent and a defibrillation safety margin of 10 J is usually easily established [14].

Defibrillation threshold testing at the time of ICD implant is currently the standard of care. However, there are clinical situations where induction of ventricular fibrillation (VF) may be associated with negative outcomes. This would include significant hypotension, respiratory distress, acute congestive heart failure, known large ischemic burden and left atrial thrombus in the setting of atrial fibrillation. When implant DFT testing is not performed, programmed shock strength is usually set to maximal output. There is very little published data to our knowledge that describes the clinical outcomes in patients who do not undergo routine DFT testing at the time of ICD implantation.

The aim this study is to compare the outcomes of patients who did not undergo DFT versus those who did undergo DFT testing at implant.

Methods

A retrospective chart review was done to identify all patients who underwent ICD implantation without DFT testing at the University of Michigan between 1999 and 2004. We identified patients who did not undergo DFT testing at the time of implantation over this time period as the "No-DFT group". Patients who underwent DFT testing at implantation during the same time period were randomly identified as the DFT group. Primary outcome variables included appropriate shocks, clinical shock efficacy and all-cause mortality. Data on demographic variables, underlying cardiac disease, use of medications and reason for not testing were collected. Data on total number of shocks and appropriate therapies was also collected. Clinical Shock Efficacy was defined as shocks effective in terminating ventricular tachycardia or fibrillation.

Method of DFT testing and programmed shock energy in DFT group

In the DFT group, a step-down DFT testing protocol was used. VF was induced by T-wave shocks. In those patients in whom VF could not be induced by T-wave shock, direct current induction was performed. The vast majority of patients received an initial defibrillation test shock of 21 joules. If this shock was successful, VF was again induced and subsequent defibrillation shocks were given at 17, 14 and then 11 joules with a 5 minute waiting period between inductions. First shock energy was programmed 10 joules higher than the lowest successful defibrillation test shock.

Statistical analysis

Statistical analyses were performed using the Statistical Program for Social Sciences (version 13.0 SPSS Inc., Chicago, Illinois). Frequency analysis was done to identify the distribution of variables. An independent sample t-test was used to detect differences between continuous variables. Continuous variables are represented as the mean ± ± standard deviation. Chi-square test was used to test association between categorical variables. A Fisher's exact test was used when appropriate. A p value of < 0.05 was considered to be statistically significant. The probability of survival was estimated and graphically displayed according to the method of Kaplan and Meier, with comparison of cumulative events by the log-rank test. Cox proportional hazards regression was used to develop multivariate regression models for the endpoint of survival. It was found that the DFT covariate interacted with follow-up time and so the DFT covariate was dichotomized at 1.5 years. Based on univariate analyses and clinical correlation, the variables (gender, prior CABG, NYHA class, No-DFT testing) were included in the regression model. Due to limited data available, anti-arrhythmic use was not included in the model. Kaplan-Meier and Cox regression analyses were performed using SAS software version 9.1.3 (SAS Institute Inc, Cary, NC).

Table 1. Distribution of variables between patients who underwent defibrillation threshold (DFT) testing *vs*. those who did not at the time of ICD implantation.

Variables	No-DFT group (n = 55)	DFT group (n = 57)	P
Mean age (years)	64.1 ± 12.1	58.8 ± 13.9	0.06*
Female	15 (27.8%)	9 (15.8%)	0.167 ^
Coronary artery disease	39 (70.9%)	39 (68.4%)	0.775#
Prior coronary artery bypass grafting	23 (42.6%)	14 (24.6%)	0.044#
NYHA class III + IV	40 (78.4%)	24 (47.1%)	0.001#
Duration of follow up	540.16 ± 521.6	525.58 ± 377.11	0.865*
ACE inhibitor	41 (77.4%)	45 (78.9%)	0.84#
Beta blocker	36 (67.9%)	42 (73.7%)	0.51#
Digoxin	39 (75%)	23 (40.4%)	0.001#
Amiodarone	16 (69.6%)	13(22.8%)	0.001#
Ejection fraction	20.98 ± 12.48	25.12 ± 11.33	0.076*
ICD indications			0.332#
Ventricular tachycardia	10 (18.2%)	12 (21.1%)	
Ventricular fibrillation	6 (10.9%)	4 (7.0%)	
NSVT¶	17 (30.9%)	24 (42.1%)	
Low ejection fraction¶	11 (20%)	7 (12.3%)	
MADIT II	8 (14.5%)	10 (17.5%)	
Infiltrative	1 (1.8%)	0	
Not documented	2 (3.6%)	0	

*p based on t-test, #p based on χ^2, ^ Fischer exact test, ¶plus inducible sustained ventricular tachycardia/syncope

Results

Table 1 compares the baseline characteristics in the No-DFT and DFT groups. The mean age of the No-DFT group (n = 55) was slightly higher than that of the DFT group (n = 57) (64 ± 12 years *vs*. 58 ± 13 years, p = 0.06). The distribution of gender was similar between the No-DFT group and the DFT group (27.8% women *vs*. 15.8% women, p = 0.125). Patients in the No-DFT group were followed for a mean of 540 ± 521 days *vs*. 525 ± 377 days for the DFT group (p = 0.865). Although the prevalence of CAD was similar between the DFT group and the No-DFT group (68.4% *vs*. 70.9%, p = 0.775), a higher percentage of the No-DFT group had a history of congestive heart failure (78.4% of No-DFT group *vs*. 47.1% of DFT group, p = 0.001). The mean ejection fraction was higher in the DFT group compared to the No-DFT group (25 ± 11 *vs*. 20 ± 12, p = 0.076). Significantly more patients in the No-DFT group had prior CABG as compared to the DFT group (42.6% *vs*. 24.6%, p = 0.044). The distribution of medications such as ACE inhibitors (p = 0.84) and beta blockers (p = 0.51) were not significantly different between the No-DFT and the DFT groups. The use of digoxin and amiodarone were both higher in the No-DFT group as compared to the DFT group and these differences were statistically significant (p = 0.001). The indications for ICD implantation are also listed in Table 1.

The characteristics of the implanted devices including manufacturers, system type, pacing threshold, sensing and lead impedance are listed in Table 2. The most common reasons for not performing DFT testing at the time of implant were hypotension (34.5%), AF and inability to exclude left atrial thrombus (27.3%), left ventricular thrombus (5.5%), CHF (7.3%), ischemia (7.3%), and others as listed in Table 3. There were no patients in the DFT group who did not have at least a 10 joule safety margin between lowest successful defibrillation test shock and programmed first shock energy.

The total number of shocks (51 in No-DFT group *vs*. 54 in DFT group, p = 0.57) and total appropriate treatments (46 *vs*. 48, p = 0.19) did not differ between the two groups. Of the 51 shocks in the study population, 91.7% were appropriate therapies as compared to 94.1% appropriate therapies in the DFT group (p = 0.99). All appropriate therapies did result in termination of the underlying ventricular tachyarrhythmia. Of the patients who did not undergo DFT testing, 69.1% were alive during follow up as compared to 91.2 % in the DFT group (p = 0.004). There was a higher percentage of patients with episodes of ventricular fibrillation in the No-DFT group as compared to the DFT group (9.1% *vs*. 3.1%, p = 0.037) (Table 4).

Table 2. Characteristics of device implants.

	No-DFT group (n = 55)	DFT group (n = 57)	P
Device manufacturers			< 0.001#
Guidant	34 (60.7%)	46 (80.7%)	
Medtronic	14 (25%)	9 (15.8%)	
Ventak	7 (12.5%)	0	
Unknown	1 (1.8%)	2 (3.5%)	
System type			< 0.001#
Single	24 (42.9%)	46 (80.7%)	
Dual	24 (42.9%)	8 (14.0%)	
Unknown	8 (14.3%)	3 (5.3%)	
Pacing threshold	0.91 ± 0.66	0.77 ± 0.58	0.236*
Pace Impedance	679.8 ± 230.8	832.6 ± 335.2	0.007*
R wave amplitude [mV]	12.08 ± 6.3	12.84 ± 6.2	0.549*

*p based on t-test, #p based on χ^2; DFT — defibrillation threshold

Table 3. Comorbid conditions responsible for not performing defibrillation threshold (DFT) testing at the time of ICD implantation in the No-DFT group.

Comorbid conditions	Number (percent)
Hypotension	19 (34.5%)
Atrial fibrillation with no pre-procedure TEE	15 (27.3%)
Coronary heart failure	4 (7.3%)
Left ventricular thrombus	3 (5.5%)
Hyperkalemia	1 (1.8%)
Ischemia	4 (7.3%)
Non revascularized left anterior descending	1 (1.8%)
Perforation/pericardial tamponade	1 (1.8%)
Prolonged procedure	2 (3.6%)
Risk of ventricular fibrillation	1 (1.8%)
Severe aortic stenosis	1 (1.8%)
Ventricular fibrillation non inducible	2 (3.6%)
Unknown	1 (1.8%)

Cause specific mortality data was available in 19/22 (86.3%) patients (Table 5). Kaplan Meier survival curves are represented in Figure 1. A significant survival benefit was noted in patients who underwent DFT testing compared to the No-DFT group (p = 0.028). Cox regression analysis showed that the No-DFT group had a significantly higher hazard ratio to predict mortality before adjusting for other factors (HR 4.59, 95% CI 1.3–16.28, p = 0.018). The final regression model after adding other variables showed several independent predictors of mortality including No-DFT testing (HR 3.18, 95% CI 0.82–12.41, p = 0.095) and NYHA (HR 2.59, 95% CI 0.79–8.45, p = 0.115). Male gender (HR 0.47, 95% CI 0.18–1.27, p = 0.136) and history of prior CABG (HR 0.64, 95% CI 0.21–1.96, p = 0.43) appeared to be protective (Table 6). There were more deaths attributable to VF in the No-DFT group (3 of 17 deaths, 17.6%) as compared to the DFT group in which no deaths from VF were recorded.

Table 4. Differences in outcomes between patients who underwent defibrillation threshold (DFT) testing *vs*. those who did not at the time of ICD implantation.

	No-DFT group (n = 55)	DFT group (n = 57)	P
Number of patients alive	38 (69.1%)	52 (91.2%)	0.004 ^
Recorded arrhythmias			0.037
NSVT	0	5 (8.8%)	
Ventricular tachycardia	7 (12.7%)	13 (22.8%)	
Ventricular fibrillation	5 (9.1%)	2 (3.1%)	
None	43 (78.2%)	37 (64.9%)	
Clinical shock efficacy	11 (91.7%)	16 (94.1%)	0.99 ^
Total shocks	51	54	0.57*
Total arrhythmic episodes treated	46	48	0.19*

*p based on t-test, ^ Fischer exact test

Table 5. Cause specific mortality between patients who underwent defibrillation threshold (DFT) testing *vs*. those who did not at the time of ICD implantation.

Causes	No-DFT group (n = 17)	DFT group (n = 5)
Acute myocardial infarction	0	1 (20 %)
Aspiration pneumonia	0	1 (20%)
ESRD	1 (5.9%)	0
Refractory coronary heart failure	8 (47.1%)	1 (20%)
Sepsis	3 (17.6%)	0
Ventricular fibrillation	3 (17.6%)	0
Unknown	2 (11.8%)	2 (40%)

P value based on χ^2 test based on double variables was 0.081

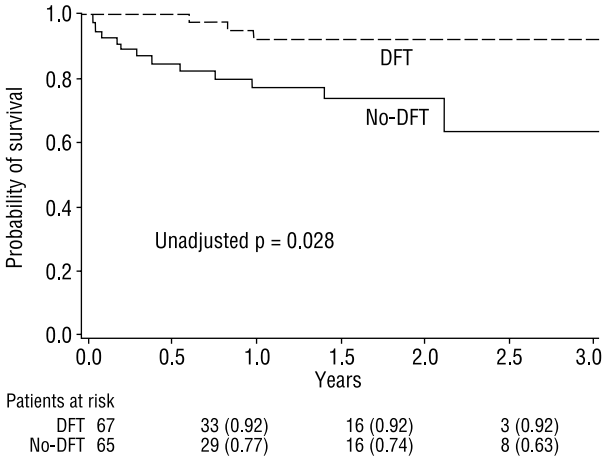

Figure 1. Kaplan-Meier survival analysis curves in patient who underwent defibrillation threshold (DFT) testing and those who did not have DFT testing at the time of ICD implantation.

Discussion

Several recent studies have looked at the need for routine DFT testing at the time if ICD system implantation [15–17]. In addition to increasing costs, induction and termination of VF can be associated with increased morbidity [19–21]. Multiple VF inductions at the time of ICD implantation with higher defibrillation energy requirements has been associated with higher mortality rates during follow-up [15]. While Brunn et al. [16] reported a 0.4% failure of ICD during routine tests, Russo et al. [18] reported an inadequate safety margin in 6% of patients undergoing ICD implantation.

In this study, we compared the clinical outcomes in patients who underwent routine DFT implant testing with those patients in whom DFT testing was precluded by their other clinical comorbidities. In our study, there was a survival benefit for patients who underwent DFT testing. This is perhaps not surprising given the No-DFT group likely represented a sicker group of patients who were believed to be at increased risk for VF induction. However, multivariate analysis revealed several variables including No-DFT testing as independent predictor of mortality. In addition Kaplan--Meier curves showed a survival benefit even from very early follow-up. There were more deaths attributable to VF in the No-DFT group (3/17 deaths 17.6%). We were unable to obtain ICD intracardiac electrograms after the deaths of these patients. Thus, we do not know if these arrhythmic events represented failed therapy versus exhaustion of ICD therapy with no termination of the arrhythmia. Our study findings are of significant interest because the need for routine DFT testing at the time of ICD implant is being questioned.

While some studies have favored routine DFT testing at the time of ICD implantation [17, 18], others have questioned the utility in testing every patient [16]. Untreated ventricular tachyarrhythmias due to programming errors have been reported and implicated as the cause of sudden cardiac death in some patients [22]. It is certainly also possible for leads to be misplaced or not inserted all the way to the distal set screw leading to inappropriate or ineffective shock therapy. It is for these reasons that performing DFT testing at the time of ICD implantation remains the standard of care.

While most patients tolerate VF induction and termination, implant DFT testing can be associated with negative clinical outcomes such as significant

Table 6. Cox regression analysis: Predictors of all cause mortality.

Variables	Hazard ratio	95% confidence interval	P
No defibrillation threshold	3.18	0.82–12.41	0.095
Male gender	0.47	0.18–1.27	0.136
NYHA	2.59	0.79–8.45	0.115
Coronary artery bypass grafting	0.64	0.21–1.96	0.43

hemodynamic compromise [21]. Therefore, certain patients who have other co-morbidities often do not undergo DFT testing. When DFT testing is not performed, first shock energy is usually programmed to maximal output. However, Russo et al. [18] showed that use of high shock energy output (≥ 35 J) alone did not allow for an adequate safety margin in 3% of their study population. Further device system modification to achieve adequate DFT did not result in a mortality difference [18].

There are few studies that have looked at the outcomes in patients who did not undergo DFT testing at the time of ICD implantation. Thus, it is impossible to know what the long term clinical outcomes would be if implant DFT testing was eliminated all together. Pires et al. [23] found in their retrospective analysis that patients who did not undergo intraoperative defibrillation testing had significantly higher overall mortality rates than those who underwent either DFT or defibrillation safety margin testing. However, the three groups had comparable successes of ICD therapies against spontaneous VT/VF and sudden-death-free survival rates. The results of our study would corroborate these findings. Strickberger et al. [14] point to the fact in their review that eliminating DFT testing may allow non electrophysiologists to implant defibrillators allowing for a greater number of patients to be reached that may benefit from ICD therapy. However our study results favors DFT testing or at least safety margin testing should be done when feasible. A much larger prospective randomized trial would need to be conducted prior to making any such conclusions.

Limitations of this study include non-randomization, smaller sample size and shorter duration of follow up. We were also unable to determine the cause of death in 13.7% of patients. It is possible that a portion or all of these deaths were arrhythmic deaths which could affect the results of this study. Also, adjusting for severity of illness between the two groups may be imperfect. This is especially true given the relatively smaller number of deaths which limits the power of regression analysis to detect the predictors of death. The mean differences in age between the two groups, although statistically not significant should be noted. Also case control study design is inferior to randomized clinical trial to prove causality. Ideally controls should be matched with age, gender and co-morbidities and our data has a higher percentage of co-morbidities in the No-DFT group which could bias the results.

Conclusions

In summary, the overall mortality was higher in the No-DFT group even after adjusting for other clinical variables. There were more episodes of VF and deaths attributable to VF in the No-DFT group. These findings suggest that DFT testing should remain the standard of care until we have further data from large randomized trials. However, ICD therapy should not be withheld in patients who meet appropriate implant criteria simply of the basis of clinical scenarios that preclude routine DFT testing.

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