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Predictive Value of Microvolt T-Wave Alternans in Patients With Left Ventricular Dysfunction

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Objectives The purpose of this study was to prospectively evaluate the utility of microvolt T-wave alternans (TWA) in predicting arrhythmia-free survival and total mortality in patients with left ventricular (LV) dysfunction.

Background Microvolt TWA has been proposed as a useful tool in identifying patients unlikely to benefit from prophylaxis with implantable cardioverter-defibrillator (ICD) prophylaxis.

Methods We evaluated 286 patients with an LV ejection fraction ≤35% who underwent TWA and electrophysiologic testing (EPS) owing to nonsustained ventricular tachycardia and/or syncope. Positive and indeterminate TWA results were grouped as non-negative. The primary end point was arrhythmia-free survival; the secondary end point was all-cause mortality.

Results Patients were followed for a mean of 38 ± 11 months. There was no significant difference between the TWA-negative (n = 90; 31%) and non-negative (n = 196; 69%) groups with respect to ICD implant rates (54% vs. 64%, respectively; p = 0.95) or etiology of cardiomyopathy (ischemic: 73% vs. 76%; p = 0.71). The Kaplan-Meier curves demonstrated improved arrhythmia-free survival in TWA-negative patients (81% vs. 66% at 2 years; p < 0.001), including in both ischemic (79% vs. 64% at 2 years; p = 0.004) and nonischemic (88% vs. 71% at 2 years; p = 0.015) subgroups. Total mortality was lower in the TWA-negative group (10% vs. 18% at 2 years; p = 0.04). The negative predictive value of TWA for (2-year) total mortality was 90%, and 83% for EPS.

Conclusion Microvolt TWA predicts arrhythmia-free survival among patients with LV dysfunction. However, the event rate in the TWA-negative group suggests that TWA may not be capable of identifying a sufficiently low-risk subset in this population to obviate the need for ICD implantation. (J Am Coll Cardiol 2007;50:166–73) © 2007 by the American College of Cardiology Foundation

Sudden cardiac death is responsible for over 400,000 deaths in the U.S. annually and is mostly attributable to ventricular arrhythmias (1). Within the past decade, microvolt T-wave alternans (TWA) testing has emerged as a potential means of risk-stratifying patients with respect to sudden cardiac death (2–5). Although large clinical trials such as the SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) (6) and the MADIT-II (Multicenter Automatic Defibrillator Implantation Trial II) (7) have demonstrated a survival benefit with prophylactic implantable cardioverter-defibrillator (ICD) implantation in patients with left ventricular (LV) dysfunction, the substantial cost of ICD implantation and relatively high number that need to be treated to save one life suggest that further risk stratification could be useful (8–10).

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Electrophysiologic studies (EPS) have been used in the risk stratification for sudden death. This is partially based on the MADIT study (11) of postmyocardial infarction patients with reduced LV function and nonsustained ventricular tachycardia (VT), demonstrating a survival benefit among ICD recipients who were inducible for sustained VT. However, arrhythmic event rates were sufficiently high

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among the noninducible patients in the MUSTT (Multicenter Unsustained Tachycardia Trial) registry (12) to raise concerns about its negative predictive value in this patient population. Furthermore, the role of EPS in relation to microvolt TWA testing, as well as their relative effectiveness as screening tools remains unclear. There is a paucity of prospective data comparing the 2 concomitantly among patients with LV dysfunction.

The purpose of the present study was to better define the prognostic value of microvolt TWA among patients with left ventricular dysfunction to determine whether TWA can identify sufficiently low-risk patients unlikely to benefit from a prophylactic ICD implantation. We also sought to compare TWA with EPS in their ability to risk-stratify this patient population. Therefore, we designed a prospective observational study to evaluate the utility of TWA in predicting arrhythmia-free survival in patients with LV dysfunction (LV ejection fraction [EF] ≤35%) among patients who underwent both EPS and TWA for sudden cardiac death risk-stratification.

Abbreviations and Acronyms

EF = ejection fraction
EPS = electrophysiology study
ICD = implantable cardioverter-defibrillator
LV = left ventricle/ventricular
LVEF = left ventricular ejection fraction
NPV = negative predictive value
NYHA = New York Heart Association
TWA = T-wave alternans
VT = ventricular tachycardia

Methods

Study population and design. We prospectively screened 650 patients who underwent simultaneous EPS and TWA for evaluation of nonsustained VT and/or syncope, between January 1, 2001, and December 31, 2003, at our institution. Patients were eligible if they were at least 18 years old, gave informed consent, and were in sinus rhythm at the time of evaluation. Patients with LV dysfunction as defined by LVEF ≤35% were included in the study, regardless of etiology of cardiomyopathy. Patients with a history of sudden cardiac death or sustained ventricular arrhythmias were excluded. The primary composite end point, arrhythmia-free survival, was defined as freedom from death or sustained ventricular arrhythmias (VT or ventricular fibrillation [VF]). Ventricular tachycardia was defined as sustained if the episode lasted for ≥30 s, or required cardioversion or appropriate ICD shock. The secondary end point was all-cause mortality. The study was approved by our Institutional Review Board.

Cardiomyopathy classification. Cardiomyopathy was determined to be ischemic in origin if any of the following criteria were met: 1) stenosis of a major epicardial coronary artery of ≥70%; 2) history of coronary artery bypass graft surgery; 3) history of percutaneous cardiovascular revascularization; or 4) documented prior myocardial infarction. All other patients were deemed to have cardiomyopathy due to a nonischemic etiology.

Electrophysiologic study. After giving informed written consent, patients underwent electrophysiologic evaluation after an overnight fast. Patients were locally anesthetized using 0.25% bupivacaine and minimally sedated with intravenous midazolam, morphine, and/or fentanyl. Quadripolar 6-F catheters were advanced from the femoral veins to the high right atrium, His bundle position, and right ventricular apex and/or outflow tract. Bipolar intracardiac electrograms were filtered at 30 to 500 Hz. The stimulation protocol included burst atrial and ventricular pacing and the introduction of single atrial and up to triple ventricular extrastimuli from 1 or 2 right ventricular sites. Stimuli were delivered as rectangular pulses of 2-ms duration at 4 times diastolic threshold. A positive EPS was defined as sustained monomorphic VT inducible with up to triple extrastimuli or polymorphic VT or VF inducible with up to double extrastimuli in the basal state.

Microvolt TWA testing. Evaluation of microvolt T-wave alternans was performed during atrial pacing at the time of electrophysiologic study, as previously validated (13). Careful skin preparation included mild abrasion and placement of high-resolution electrodes (High-Res, Cambridge Heart, Bedford, Massachusetts). Electrocardiographic leads were placed in the standard 12-lead and orthogonal X, Y, and Z configurations. The protocol involved measurement during right atrial pacing at cycle length of 550 ms for 5 min. The TWA was analyzed using either the CH2000 or the HearTwave system (Cambridge Heart). A positive test was defined as TWA sustained for ≥1 min with alternans voltage (Valt) ≥1.9 μV and TWA ratio ≥3.0, according to previously published criteria (14). A negative test was defined as the absence of significant TWA (i.e., ≤1.9 μV) during atrial pacing. Causes of an indeterminate test included excessive (ventricular or atrial) ectopy, atrioventricular Wenckebach, and excessive artifact due to noise. Positive and indeterminate TWA test results were grouped as non-negative according to convention from earlier studies (14). Recent data in patients with LV dysfunction have indicated that patients with indeterminate and positive TWA tests have a similar risk of death or sustained ventricular arrhythmias (15).

Clinical follow-up. Patients were followed by routine clinic visits for device interrogation at scheduled intervals, standardized telephone interviews, and institutional hospital admissions tracked using electronic medical records. When necessary to assess end points, detailed records from outside institutions and physicians were obtained with patient consent given separately during the follow-up period. All death events were independently verified against the Social Security Death Index for precise measurement of survival time from the time of evaluation. The minimum event-free follow-up time interval required for inclusion was defined as ≥12 months, and those who did not meet this standard were considered lost to follow-up.

Statistics. Continuous variables were expressed as mean ± standard deviation, and comparisons between groups were made using the independent samples *t* test. Categoric variables, expressed as numbers and percentages, were compared using chi-square analysis. Kappa test was used to measure agreement between EPS and TWA results. Kaplan-Meier curves were constructed to describe the arrhythmia-free survival and total mortality experience for TWA negative and non-negative patients, including the presence or absence of ischemic heart disease. The log-rank test was applied for statistical significance. The Cox proportional hazards model was applied to assess TWA results and the primary end point of arrhythmia-free survival, as expressed by a hazard ratio (HR) with a 95% confidence interval (CI). A corresponding analysis was performed using Cox regression to investigate potential confounding variables for interaction with TWA results. Candidate variables included age, gender, LV function, New York Heart Association (NYHA) functional classification, QRS duration, use of beta-blockers, cardiomyopathy etiology, EPS result, ICD implantation, and TWA testing. These variables were considered individually and collectively, with p values based on the Wald test from the Cox models. For all tests, p values of <0.05 were considered to be significant. Data analysis was performed using SPSS for Windows v10.1 (SPSS Inc., Chicago, Illinois).

Results

During the enrollment period, 344 patients met the criteria for LV dysfunction (EF ≤35%), and 36 of these were subsequently excluded based on a history of sudden cardiac death or sustained ventricular arrhythmias. Among the 308 remaining eligible patients, 20 were lost to follow-up and 2 subsequently withdrew consent during the follow-up period. Overall, 286 of the 308 eligible patients (93%) were followed up for a mean of 38 ± 11 months.

The baseline clinical characteristics of the 286 patients are detailed in Table 1. The mean age was 65 ± 11 years, and 224 (78%) were male. Two hundred fourteen patients (75%) had an ischemic cardiomyopathy, and 72 (25%) had a nonischemic cardiomyopathy. The average LVEF of the group was 26 ± 7%. One hundred forty-five patients (51%) had a normal QRS, 67 (23%) had evidence of intraventricular conduction delay (QRS 110 to 120 ms), and 74 (26%) had bundle branch block (QRS >120 ms). The NYHA congestive heart failure classification distribution at the time of the study was: 33 (12%) were class I, 135 (47%) class II, 105 (37%) class III, and 13 (5%) class IV. Two hundred thirty-seven patients (83%) were treated with beta-blockers, 207 (72%) with either an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, 133 (47%) with a statin, and 14 (5%) with amiodarone. Two hundred forty patients (84%) were referred for nonsustained VT, 23 (8%)

Table 1 Baseline Clinical Characteristics

Characteristic	All (n = 286)	TWA Negative (n = 90)	TWA Positive or Indeterminate (n = 196)	p Value
Age, yrs	65 ± 11	65 ± 11	66 ± 12	0.73
Male gender	224 (78%)	70 (78%)	154 (79%)	0.99
LVEF, %	26 ± 7	27 ± 7	26 ± 7	0.83
Ischemic cardiomyopathy	214 (75%)	66 (73%)	148 (76%)	0.71
QRS duration, ms				0.17
<110	145 (54%)	53 (59%)	92 (47%)	
110–120	67 (25%)	18 (20%)	49 (25%)	
>120	74 (28%)	19 (21%)	55 (28%)	
NYHA functional classification				0.38
I	33 (12%)	8 (9%)	25 (13%)	
II	135 (47%)	47 (52%)	88 (45%)	
III	105 (37%)	33 (37%)	72 (37%)	
IV	13 (5%)	2 (2%)	11 (6%)	
Medications				
Beta-blocker	237 (83%)	71 (79%)	166 (85%)	0.91
ACE inhibitor/ARB	207 (72%)	61 (68%)	146 (75%)	0.91
Statin	133 (47%)	41 (46%)	92 (47%)	0.90
Amiodarone	14 (5%)	2 (2%)	12 (6%)	0.24
Reason for evaluation				0.56
Syncope	23 (8%)	9 (10%)	14 (7%)	
Nonsustained VT	240 (84%)	76 (84%)	164 (84%)	
Both	23 (8%)	5 (6%)	18 (9%)	
ICD implant after EPS	174 (61%)	49 (54%)	125 (64%)	0.95

ACE = angiotension-converting enzyme; ARB = angiotensin receptor blocker; EPS = electrophysiology study; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; TWA = T-wave alternans; VT = ventricular tachycardia.

Table 2 Agreement Between TWA and EPS Results

	TWA Negative (n = 90)	TWA Non-Negative (n = 196)
All patients (kappa score 0.9)		
Total	90	196
EPS positive (n = 115)	29	86
EPS negative (n = 171)	61	110
Ischemic cardiomyopathy patients (kappa score 0.14)		
Total	66	148
EPS positive (n = 111)	27	84
EPS negative (n = 103)	39	64
Nonischemic cardiomyopathy patients (kappa score −0.03)		
Total	24	48
EPS positive (n = 16)	6	10
EPS negative (n = 56)	18	38

EPS is defined as positive only if inducible without catecholamine infusion.
Abbreviations as in Table 1.

for syncope, and 23 (8%) for both syncope and nonsustained VT.

The TWA testing was performed at the time of the EPS. The TWA was negative in 90 patients (31%) and non-negative in 196 (69%). The non-negative group included 121 positive (42%) and 75 indeterminate (26%) results. Only 5 of the indeterminate cases were due to noise (7%), with the remainder due to atrioventricular Wenckebach (23 [30%]) or excessive atrial or ventricular ectopy (47 [63%]).

The TWA-negative and −non-negative patients were comparable with respect to age, LVEF, prevalence of ischemic heart disease, NYHA functional classification, and standard cardiac medications (Table 1).

Overall, 174 patients (61%) underwent ICD implantation. There was no significant difference between the TWA-negative and −non-negative groups with respect to rates of subsequent ICD implantation (n = 49 [54%] vs. 125 [64%], respectively; p = 0.95).

Correlation between TWA and EPS. The EPS was positive in 115 patients (40%). Of those patients, 86 (75%) had a non-negative TWA result. In the 171 patients who were noninducible for VT at EPS, 61 (36%) had a negative TWA result (Table 2). Conversely, of the 90 patients with a negative TWA result, 61 (68%) had a negative EPS. In the non-negative TWA group (196 patients), 86 (44%) had a positive EPS. Therefore, 139 patients (49%) had discordant results with respect to EPS and TWA. In a bivariate analysis, there was no statistically significant agreement between EPS and TWA results (kappa value 0.09).

When looking at the agreement between EPS and TWA in patients with ischemic and nonischemic cardiomyopathy separately, there was still no strong agreement in either group, although the patients with ischemic cardiomyopathy had a slightly better concordance, as would be expected. Of the 214 ischemic cardiomyopathy patients, 111 had a positive EPS result (84 [76%] of whom had a non-negative TWA result) and 103 had a negative EPS (39 [38%] of whom had a negative TWA) (Table 2). In the 72 nonischemic cardiomyopathy patients, 16 had a positive EPS (10 [63%] of whom also had a non-negative TWA), and 56 had a negative EPS (18 [32%] of whom had a negative TWA) (Table 2). Kappa values were 0.14 for the ischemic population and −0.03 for the nonischemic population.

Survival data. Kaplan-Meier survival analysis demonstrated improved arrhythmia-free survival in TWA-negative patients compared with non-negative patients (81% vs. 66% at 2 years, respectively; $p < 0.0001$) (Fig. 1). Of note, TWA-positive and -indeterminate patients had similar rates of arrhythmia-free survival (66% vs. 65%, respectively; data not shown). All-cause mortality was also lower in the TWA-negative group than in the TWA–non-negative group (10% vs. 17% at 2 years, respectively; p = 0.04) (Fig. 2).

In univariate analysis, TWA testing was a strong predictor of the primary end point of arrhythmia-free survival (HR 2.33, 95% CI 1.44 to 3.67; $p < 0.01$). In contrast, EPS was not found to be a statistically significant predictor of arrhythmia-free survival (HR 1.27, 95% CI 0.88 to 1.83; p = 0.21). Multivariate analysis was also performed, and included age, gender, QRS duration, LVEF, NYHA congestive heart failure class, cardiomyopathy etiology (ischemic vs. nonischemic), and subsequent ICD implantation, as detailed in Table 3. There were no significant interactions between any of these variables. The TWA testing remained a significant predictor of the primary end point when adjusted for the other variables (multivariate HR 2.37, 95% CI 1.49 to 3.81; $p < 0.01$).

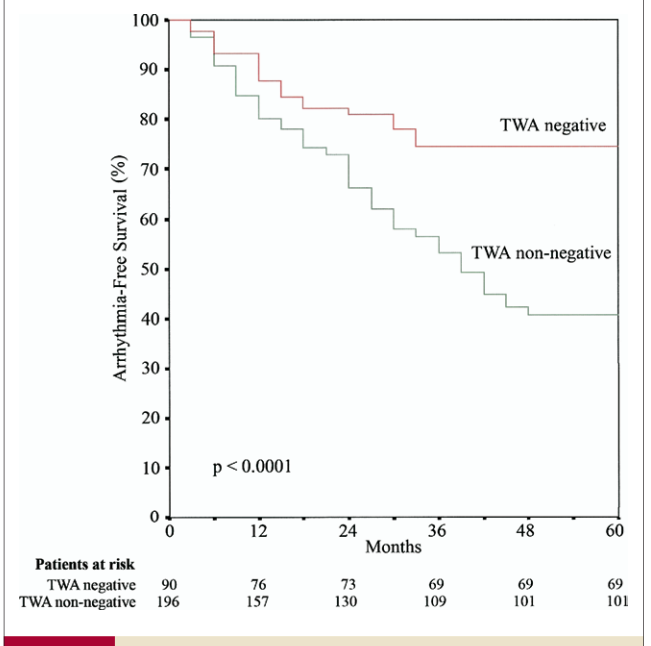


Figure 1 Kaplan-Meier Survival Curves for Arrhythmia-Free Survival

Stratified by T-wave alternans (TWA) testing result.

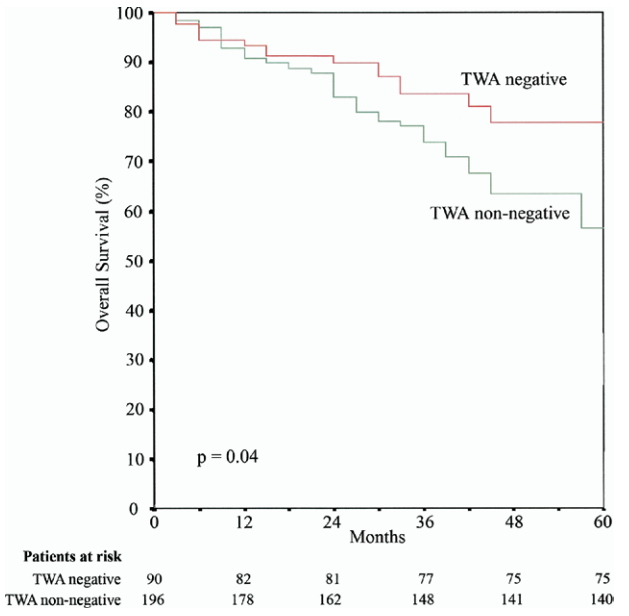


Figure 2 Kaplan-Meier Survival Curves for All-Cause Mortality

Stratified by T-wave alternans (TWA) testing result.

The arrhythmia-free survival benefit for TWA-negative versus –non-negative patients persisted when evaluated separately in the ischemic cardiomyopathy (79% vs. 64% at 2 years, respectively; p = 0.004) and nonischemic cardiomyopathy (88% vs. 71% at 2 years, respectively; p = 0.015) patient subgroups (Figs. 3A and 3B).

When stratified by both EPS and TWA results, there was a significant difference in 2-year event rates for arrhythmia-free survival (p = 0.0006) (Fig. 4); i.e., the addition of 1 test to the other added to the negative predictive value. The 2-year event rates were as follows: 1) EPS and TWA negative: 15% (n = 61); 2) EPS positive and TWA negative: 28% (n = 29); 3) EPS negative and TWA–non-negative: 35% (n = 110); and 4) EPS positive and TWA–non-negative: 33% (n = 86).

Discussion

The present results demonstrate that, compared with electrophysiologic evaluation, microvolt TWA testing is a more effective predictor of arrhythmia-free survival and all-cause mortality in patients with nonsustained VT and/or syncope.

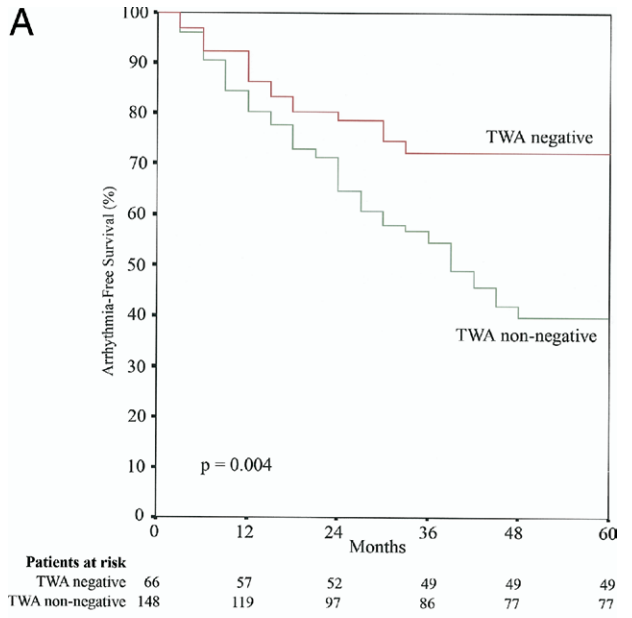
Although our findings are concordant with earlier observational studies (16–19) that evaluated the utility of TWA,

Table 3 2-Year Event Rates and Univariate Hazard Ratios

Variable*	n	2-Year Events (%)	Univariate HR (95% CI)	p Value
Age				
≥65 yrs	155	31.3	1.07 (0.73–1.57)	0.71
<65 yrs	131	29.3		
Gender				
Female	62	24.7	0.64 (0.38–1.08)	0.09
Male	224	30.9		
LVEF				
≤30%	134	30.5	1.05 (0.71–1.56)	0.81
>30%	152	29.5		
QRS duration (ms)				
≥120	74	35.0	1.00 (0.62–1.62)	0.16
<120	212	27.4		
NYHA functional class				
III or greater	118	35.0	1.39 (0.91–2.10)	0.13
II or less	168	27.8		
Beta-blockers				
Yes	237	27.5	0.79 (0.46–1.15)	0.17
No	49	39.9		
Cardiomyopathy				
Ischemic	214	30.9	1.04 (0.66–1.67)	0.85
Nonischemic	72	20.4		
EPS				
Positive	115	40.2	1.27 (0.88–1.83)	0.20
Negative	171	59.8		
Microvolt TWA*				
Non-negative	196	34.3	2.33 (1.44–3.67)	<0.01
Negative	90	19.1		

All p values are based on Wald test. *Adjusted HR 2.37 (95% CI 1.49 to 3.81; p < 0.01) for TWA result and primary end point of arrhythmia-free survival after adjustment for the other table variables listed in multivariate analysis using Cox models. None of the other interactions examined were statistically significant.

CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.



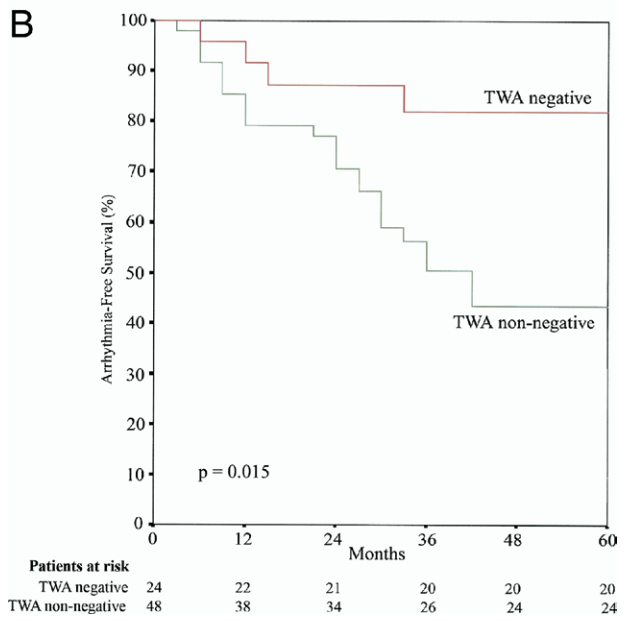


Figure 3 **Kaplan-Meier Survival Curves for Arrhythmia-Free Survival**

Stratified by T-wave alternans (TWA) testing result and subgrouped by etiology of cardiomyopathy: **(A)** ischemic cardiomyopathy patients; **(B)** nonischemic cardiomyopathy patients.

the present results demonstrate substantially higher event rates in the TWA-negative group. Using 1-year negative predictive value (NPV) for arrhythmia-free survival as a common end point for comparison, the present study demonstrated an NPV for TWA of 85%, compared with 94% in a recent series of patients with cardiomyopathy and EF ≤40%, (16) and with 92% in a series of patients with ischemic cardiomyopathy and EF ≤35% (17). In contrast with those series, the present patients were referred for evaluation specifically based on the presence of nonsustained VT and/or syncope, thus suggesting a potentially higher-risk patient population, resulting in a higher rate of clinical events. In fact, 16% of our patients were evaluated for syncope, one-half of whom also had nonsustained VT. Furthermore, both of the earlier studies excluded NYHA functional class IV patients, who were not excluded from the present series (although they comprised a small minority), to assess the utility of TWA testing across the broad spectrum of patients with congestive heart failure. The combination of these inclusion criteria may have resulted in a higher arrhythmia risk in the present group than in the previously studied low-risk primary prevention cohorts.

In the present study, EPS failed to predict the primary end point of arrhythmia-free survival, whereas TWA testing was a strong predictor in both univariate and multivariate analyses. The superiority of TWA testing in this population is likely due at least in part to the low inducibility rates during EPS of nonischemic cardiomyopathy patients. In addition, this is consistent with earlier data, which has demonstrated the suboptimal negative predictive value of EPS. In the MUSTT registry, for example, patients with a negative EPS still had 2-year rates of death of 21% and of cardiac arrest or arrhythmic death of 12% (12). In the present series, subgroup analysis of the ischemic and nonischemic patients demonstrated that TWA testing appears to be robust in both cohorts.

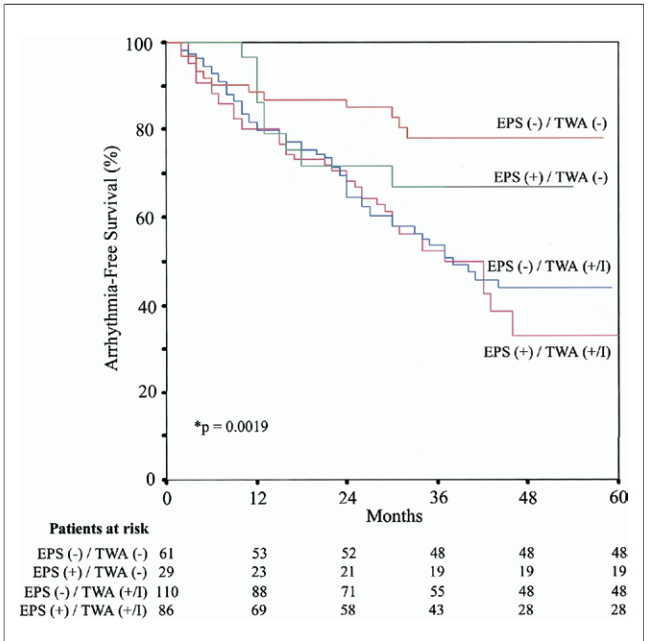


Figure 4 **Kaplan-Meier Survival Curves for Arrhythmia-Free Survival**

Stratified according to both electrophysiology study (EPS) and T-wave alternans (TWA) results. EPS (−) = EPS negative for inducible sustained ventricular tachycardia (VT); EPS (+) = EPS positive for inducible sustained VT; TWA (−) = TWA negative; TWA (+/I) = TWA positive or indeterminate (non-negative).

Discordance between TWA and EPS. Our results also highlight the fact that, although TWA and EPS can both be used to potentially risk-stratify patients for sudden cardiac death, they identify different patient population sets. Almost one-half of the present patients had discordant results with respect to TWA and EPS (i.e., non-negative TWA but negative EPS or negative TWA but positive EPS). However, it is important to highlight the fact that having both a negative TWA and negative EPS was associated with a favorable 2-year NPV for freedom from death or sustained ventricular arrhythmia (85%), which was better than with either test alone (Fig. 4).

Implications for ICD implantation. Over 90% of the patients in the present series would have met current criteria for ICD implantation (with or without cardiac resynchronization therapy). An important finding in this series is the 2-year rate of 19% for the primary end point (of death or sustained ventricular arrhythmias) among the TWA-negative patients. This suggests that the TWA test alone may not be capable of identifying a sufficiently low-risk subset in this particular population to obviate the need for ICD implantation. The addition of another test, such as EPS in the present study, may improve the (combined) NPV sufficiently to stay below the threshold for ICD implantation. This approach also appears promising based on the results of a published study examining patients with chronic ischemic heart disease (20). The NPV of a test is dependent on the pretest probability for a particular event. In the present study, it is possible that the inclusion criteria (nonsustained VT and/or syncope along with significant LV dysfunction) created a relatively high-risk cohort for ventricular arrhythmias. Further prospective randomized studies will be needed to evaluate whether the NPV of TWA would be sufficiently high in patients of the population included in our study as well as in a group without certain potentially high-risk clinical markers (e.g., syncope or nonsustained VT, different degrees of LV dysfunction) to eliminate the need for ICD implant. Any future algorithm for ICD implantation using the results of TWA testing merits evaluation in a randomized prospective clinical trial.

Study limitations. This was an observational study rather than a randomized controlled trial. As such, ICD implantation was at the discretion of the electrophysiologist, and was not randomized. However, previous TWA studies have also been observational, and withholding ICD therapy to patients who meet current implant indications would be problematic. To mitigate the effect of this, we reported arrhythmia-free survival as well as all-cause mortality. Of note, ICD implant rates were not significantly different between TWA-negative and –non-negative groups.

Also, the present study was performed using an atrial pacing protocol. Comparisons with earlier studies using a treadmill TWA protocol should be made with caution. Differences in autonomic tone, incidence of excessive artifact leading to an indeterminate result, and the ability to reach and maintain a sufficient heart rate might differ between the 2 protocols. One published series suggests that exercise testing might be superior for the risk stratification of patients with ischemic LV dysfunction (21). However, in that study the selection of exercise vs. pacing T-wave alternans evaluation was not randomized, and episodes of VT treated with antitachycardia pacing were included in the end point. Furthermore, although the authors found that exercise TWA (but not pacing TWA) was a significant predictor of events, the NPVs of the 2 modalities were almost identical.

Conclusions

Microvolt TWA predicts arrhythmia-free survival for patients with LV dysfunction (EF ≤35%) who present with nonsustained VT and/or syncope. Furthermore, it appears to be a robust predictor among patients with both ischemic and nonischemic cardiomyopathy across a broad spectrum of clinical heart failure. In patients with LV dysfunction, it outperforms EPS in predicting arrhythmia-free survival. However, in this population, the relatively high clinical event rate in the TWA-negative group suggests that TWA testing alone may not be capable of identifying a sufficiently low-risk subset to obviate the need for ICD implantation in patients with cardiomyopathy and nonsustained VT and/or syncope. The addition of another risk-stratifying modality, such as EPS, may allow for a sufficiently high NPV for arrhythmia-free survival. (18,19).

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