

Medical Policy Manual

Topic: T-Wave Alternans

Date of Origin: February 15, 2001

Section: Medicine

Last Reviewed Date: June 2014

Policy No: 88

Effective Date: September 1, 2014

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

T-wave alternans refers to a beat-to-beat variability in the amplitude of the T wave. A routine electrocardiogram (EKG) cannot detect these small fluctuations, and thus this test requires specialized sensors to detect the fluctuations and computer algorithms to evaluate the results. T-wave alternans is a provocative test that necessitates gradual elevation of the heart rate to above 100 beats per minute. The test can be performed in conjunction with an exercise tolerance stress test. Test results are reported as the number of standard deviations by which the peak signal of the T-wave exceeds the background noise. The number is referred to as the "alternans ratio." An alternans ratio of 3 or greater is typically considered a positive result; an absent alternans ratio is considered a negative result; and anything in between is considered indeterminate.

The presence of T-wave alternans has been investigated as a risk factor for fatal arrhythmias and sudden cardiac death in patients with a history of myocardial infarction or cardiomyopathy. High-risk patients may be treated with drugs to suppress the emergence of arrhythmias or undergo implantation of cardiac defibrillators to promptly terminate tachyarrhythmias when they occur. Since sudden cardiac death is one of the most common causes of death after a myocardial infarction (MI) or in patients with dilated cardiomyopathy, there is intense interest in risk stratification in order to target therapy.

Patient groups are categorized into those who have not experienced a life-threatening arrhythmia (primary prevention) and those who have (secondary prevention). Those who have already experienced a life-threatening arrhythmia are already at high risk and would not be considered for testing. T-wave

alternans testing is just one of many risk factors that have been investigated for identifying candidates for primary prevention. Others include left ventricular ejection fraction, arrhythmias detected on Holter monitor or electrophysiologic studies, heart rate variability, and baroreceptor sensitivity. Signal-averaged ECG (SAECG) is another technique for risk stratification. SAECG, addressed separately in medical policy [Medicine 21](#), measures beat to beat variability.

T-wave alternans has also been investigated as a diagnostic test for patients with syncope of unknown origin and as a non-invasive test to identify candidates for further invasive electrophysiology testing of the heart.

MEDICAL POLICY CRITERIA

T-wave alternans is considered **investigational** for all indications, including, but not limited to risk stratification for primary* or secondary** prevention of fatal arrhythmias and sudden cardiac death.

*Primary prevention refers to patients who have not experienced a life-threatening arrhythmia.

**Secondary prevention refers to patients who have experienced a life-threatening arrhythmia.

SCIENTIFIC BACKGROUND^[1]

Validation of the proposed use of T-wave alternans for identifying patients who are at increased risk for a cardiac events in comparison of to the standards of care must fulfill 3 parameters:

1. Demonstration of technical feasibility, including assessment of its reproducibility and precision. For comparison among studies, a common standardized protocol is necessary.
2. Demonstration of diagnostic performance (sensitivity, specificity, positive and negative predictive values) of breast duct endoscopy compared with the gold standard test for each proposed indication.
3. Demonstration of clinical utility of a diagnostic technique, i.e., how the results of the study can be used to benefit patient management, is established. The clinical utility of both positive and negative tests must be established.

In order to identify any additional benefit from T-wave alternans, randomized controlled trials (RCTs) are needed comparing the outcomes of patients evaluated for T-wave alternans as part of their diagnostic workup compared with patients who were evaluated with standard diagnostic tests or risk stratification tools. Evidence from non-randomized studies is not considered sufficient to reach reliable conclusions due to significant methodological limitations, such as lack of adequate control groups. Studies lacking adequate control groups cannot control for the many types of bias that may affect the treatment outcomes under investigation.

Recent primary prevention implantable cardioverter defibrillator (ICD) trials (e.g., MADIT-II and SCD-HeFT) have changed the perspective on selection and risk stratification for implantable defibrillators. In the MADIT-II trial,^[2] implantable defibrillators were shown to be effective in patients selected solely on the basis of prior myocardial infarction and reduced ejection fraction. Prior studies of implantable defibrillators had selected patients using results of electrophysiologic testing and symptoms.^[3,4] Given these specific clinical trials, it becomes critical whether any risk stratification test is a useful or efficient

maneuver in improving identification of patients who benefit or do not benefit from therapy. For example, can T-wave alternans testing identify patients who would otherwise qualify for an implantable defibrillator but who would actually not benefit from the procedure? Or alternatively, can T-wave alternans testing identify patients who do not qualify for an implantable defibrillator under the selection criteria of these clinical trials but would nonetheless benefit? However, clinical trials extending the benefits of ICD to newly identified groups of patients do not exist.

The rationale for T-wave alternans testing is primarily that patients with a negative result would not benefit from ICD placement. Accordingly, the most convincing evidence would be obtained from a randomized trial restricted to alternans-negative patients.

Literature Appraisal

To date, the primary evidence on T-wave alternans consists only of non-randomized studies. Following is a summary of the evidence published to date.

Technology Assessments

2005 BlueCross BlueShield Association (BCBSA) Technology (TEC) Assessment

A 2005 BCBSA TEC Assessment evaluated the use of T-wave alternans to risk stratify patients being considered for ICD therapy for primary prevention.^[5] The TEC Assessment identified 18 studies using T-wave alternans to prospectively stratify the risk of a subsequent event (total N=2,931). Most studies interpreted T-wave alternans blinded to other information. The prevalence of endpoint events (either VTE or death) ranged from 3% to 51% across studies. Six studies included subjects with ischemic cardiomyopathy, 4 included nonischemic cardiomyopathy, and 8 included subjects selected by a variety of means such as those referred for electrophysiologic testing.

Two patient indications were considered: 1) patients eligible for ICD placement for primary prevention of sudden death and 2) patients who are not eligible for ICD placement. It is possible that the negative or positive predictive value of T-wave alternans results might be used to support decision making regarding ICD placement. Specifically, in the first patient indication, negative T-wave alternans results might be used to identify a subset of patients at low likelihood of subsequent ventricular tachyarrhythmic events (VTE) and thus unlikely to benefit from ICD placement. While a few studies did find that T-wave alternans testing had high sensitivity and high negative predictive value for risk of future VTE, there was considerable variation in diagnostic performance in the published literature. Reported sensitivity ranged from 75% to 100%, negative predictive value from 73% to 100%, and likelihood ratios for a negative test result varied between zero and 0.42. The reasons for variation in diagnostic performance characteristics are not well-established. Differences in pretest risk of VTE would most influence negative predictive value; however, it would also be important to understand whether T-wave alternans diagnostic performance might vary according to characteristics of the population such as etiology of cardiomyopathy. The diagnostic characteristics derived from these studies may not directly apply to patients who are eligible for ICD therapy.

In conclusion, the 2005 TEC Assessment found insufficient evidence to determine whether the use of T-wave alternans improves net health outcome or whether it is as beneficial as any established alternatives. Therefore, the use of T-wave alternans testing for risk stratification in patients being considered for implantable cardioverter defibrillator therapy for primary prevention of sudden death did not meet the TEC criteria.

2006 BlueCross BlueShield Association (BCBSA) Technology (TEC) Assessment

A 2006 BCBSA TEC Assessment^[6] reviewed a smaller number of studies directly relevant to the question of whether microvolt T-wave alternans (MTWA) can identify patients who would otherwise meet clinical indications for ICD therapy but whose risk of death is so low that they would not benefit from treatment. The critical piece of data is the absolute risk of arrhythmia or sudden death in those persons who have a negative T-wave alternans test, and whether it can be determined that this risk is consistent with no potential benefit from ICD therapy. Three studies were reviewed that restricted the subjects analyzed to those patients who met criteria for ICD therapy.

- Bloomfield and colleagues^[7] followed 177 patients over an average of 20 months for all-cause mortality. Hohnloser and colleagues^[8] selected ICD-eligible patients from 2 previously published studies and followed them over 2 years for sudden cardiac death or cardiac arrest. Chow and colleagues^[9] studied 768 patients who would be eligible for ICD therapy and followed them over a mean of 18 months for all-cause mortality and cause-specific mortality. Of these 768 patients, however, over half had ICD therapy, and thus only 376 patients can be assessed for natural history.

In the study by Bloomfield and colleagues^[7], for those with a negative MTWA test, the actuarial 2-year mortality rate was 3.8%. For those with a non-negative MTWA test, the actuarial 2-year mortality rate was 17.8%. Arrhythmic outcomes were not reported in this study.

- In the study by Hohnloser and colleagues^[8], patients who met MADIT II criteria were pooled from 2 previously published studies. The study reported all-cause mortality, rates of sudden cardiac death or cardiac arrest, and rates of ventricular tachyarrhythmic events. For all-cause mortality estimated at 2 years, those with negative MTWA tests had a mortality rate of 12.5%, whereas those with non-negative MTWA tests had a mortality rate of 21.4%. For the primary outcome of sudden death or cardiac arrest, those with negative MTWA tests had a 0% rate, and those with non-negative MTWA tests had a 15.6% rate. For the secondary outcome of all ventricular arrhythmic events, those with a negative MTWA test had a 5.7% rate, and those with non-negative tests had a 31.1% rate.
- In the study by Chow and colleagues^[9], 768 consecutive patients with ischemic cardiomyopathy (LVEF <35%) and no prior history of ventricular arrhythmia were followed up for a mean of 18 months. Only the 376 patients who had only medical therapy were reported. Thus these data might be biased by selection of those who chose to have ICD therapy. It appears that the MTWA-negative patients who did not receive ICD compared to the MTWA-negative patients who did receive ICD had less severe congestive heart failure (mean left-ventricular ejection fraction 0.293 vs. 0.269). At 18 months' mean follow-up, the all-cause mortality rate was 8.4% in MTWA-negative patients, and 21.8% in MTWA non-negative patients. For arrhythmic deaths, the rate was 3.4% in MTWA-negative patients, and 11.2% in MTWA non-negative patients.

The TEC Assessment argued that although T-wave alternans does stratify risk in ICD-eligible patients, this may not translate to clinical utility, or an improvement in health outcomes. A modeling study by Chan and colleagues^[10] assumed a 2.7% annual sudden death rate among MTWA-negative patients, and calculated that patients would still benefit from ICD therapy. Although modeling studies are not definitive, this study suggests that even the lower risk of arrhythmia in MTWA-negative patients is not low enough to preclude some benefit from ICD therapy.

Systematic Reviews and Meta-analyses

- Results from two meta-analyses suggest that some discrepancies in prior study results can be explained by lower predictive performance of MTWA in studies where beta-blockers were withheld prior to testing.^[11,12] The subgroup finding, although plausible, requires confirmation.
- Merchant et al. conducted a patient-level analysis identifying studies enrolling more than 100 patients studied by the spectral method.^[13] Studies with 15% or greater patients having ICDs were excluded, as were those in which 15% or more of the arrhythmic outcomes were attributed to appropriate ICD therapy. Studies (n=2) using older protocol and instruments were also excluded. Of 17 identified studies, 5 met inclusion criteria. Patients with ICDs were also excluded from the final analysis, yielding a sample of 2,883. Among patients with LVEF <35% (n=1,004) and negative MTWA testing, the annual sudden cardiac death rate was 0.9% versus 4.0% and 4.6% in the positive and indeterminate groups. The report did not state whether all selection criteria was established a priori. In addition, no sensitivity analyses were reported accounting for excluded patients and studies.
- Gupta et al. performed a study-level meta-analysis including 20 prospective cohort studies collectively enrolling 5,945 patients with MTWA obtained by the spectral method.^[14] They estimated that a negative MTWA decreased the annual fatal and non-fatal ventricular tachyarrhythmic event (VTE) rate from 5.9% to 2.6% in SCD-HeFT-like patients, and from 8.9% to 6.4% in MADIT-II-like patients. The authors concluded that spectral MTWA testing would not “sufficiently modify the risk of VTE to change clinical decisions.”
- In 2013, Chin and colleagues evaluated the ability of MTWA to predict outcome severity after ischemic cardiomyopathy (ICM) in a meta-analysis of 7 trials.^[15] Authors indicated that the non-negative group identified by MTWA showed increased rates of cardiac mortality or severe arrhythmic events. Despite the suggestion that MTWA may be a useful risk stratification tool in determining severity of ICM, none of the studies within this review demonstrated how MTWA testing was used to alter treatment management or improve health outcomes.

Randomized Controlled Trials (RCTs)

At present, there are no randomized controlled trials of either ICDs or antiarrhythmic therapy that have relied on the results of T-wave alternans as a patient selection criterion.

Nonrandomized Studies

- An observational study of ICD placement in MTWA-negative patients was published by Chow and colleagues in 2007^[16], showing a nonsignificant risk reduction (hazard ratio=0.85, p=0.73). However, this was a retrospective observational study with a relatively small sample size. Unmeasured confounding could affect the results, and the 95% confidence interval includes a hazard ratio of 0.33.
- In 2008, Gold and colleagues published results from a prospective substudy of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) that included 490 patients at 37 clinical sites.^[17] T-Wave Alternans tests were classified by blinded readers as positive (37%), negative (22%), or indeterminate (41%) by standard criteria. The primary end point was the first occurrence of any of the following events: sudden cardiac death, sustained ventricular tachycardia/fibrillation, or appropriate implantable cardioverter defibrillator discharge. During a median follow-up of 30

months, no significant differences in event rates were found between MTWA-positive or MTWA-negative patients (hazard ratio 1.24, 95% CI= 0.60 to 2.59, P=0.56) or MTWA-negative and nonnegative (positive and indeterminate) subjects (hazard ratio 1.28, 95% CI= 0.65 to 2.53, P=0.46). Similar results were obtained with the inclusion or exclusion of patients randomized to amiodarone in the analyses. The authors concluded that MTWA testing did not predict arrhythmic events or mortality in SCD-HeFT, although a small reduction in events (20% to 25%) among TWA-negative patients could not be excluded given the sample size of the study.

- The T-Wave Alternans in Patients with Heart Failure (ALPHA) Registry enrolled 446 patients with NYHA class II and III heart failure and LVEF <40% from nine centers across Italy.^[18] Heart failure etiologies included idiopathic dilated cardiomyopathy (n=326), hypertensive cardiomyopathy (n=72), valvular causes (n=9), and others (n=39). The primary endpoint was a composite of cardiac death and life-threatening ventricular arrhythmias. Mean patient age was 59 (SD 12.5) years, 78% of patients were male, and median follow-up was 19 months. MTWA results were negative in 34.6%, non-negative in 65.4% (44.8% positive, 20.6% indeterminate). The primary endpoint occurred in 29 of 292 (9.9%) patients with non-negative results, compared to 4 of 154 (2.6%) in the negative group. A survival model attempting to adjust for between-group differences in prognostic factors yielded a relative hazard of 4.0 (95% CI: 1.2 to 13.3). The test's negative predictive value through 18 months' follow-up was 97.3% (95% CI: 95.4 to 99.8). Thirty-three patients with non-negative and six with negative results received ICDs. In sensitivity analyses accounting for the impact of ICD implantation on differential event occurrence found similar results; those with ICDs had more events recorded. These findings are consistent with most prior observational research finding negative MTWA results associated with fewer arrhythmic outcomes in nonischemic cardiomyopathy (the ScD-HEFT data being an exception). Limitations of the study include lack of a randomized comparison or using MTWA results to direct ICD placement, and between-group differences in prognostic factors including age, LVEF, use of angiotensin converting enzyme inhibitors and digitalis, and QRS duration. Although the investigators attempted to control for imbalances, the number of events (n=33) was insufficient to obtain valid estimates while accounting for more than a single prognostic factor or variable reflected in the wide confidence intervals. Furthermore, ICD placement is not indicated for primary prevention among individuals with LVEF >35%. For these reasons, few conclusions can be drawn from the results.
- Alternans Before Cardioverter Defibrillator (ABCD)^[19] was a cohort study enrolling patients considered to be primary prevention candidates for ICD implantation. All patients underwent MTWA and an electrophysiological study (EPS). The primary goal was to demonstrate noninferiority of MTWA (within 10%) to EPS testing in selecting primary prevention patients for ICD implantation. A total of 629 participants were enrolled at 43 centers in the United States, Germany, and Israel with ischemic cardiomyopathy, ejection fraction <40%, and no history of cardiac arrhythmia (a primary prevention sample). Due to protocol violations, 63 participants were excluded, yielding an analytic sample of 566. Following EPS and MTWA testing ICDs were implanted if results were positive for either test. When both tests were negative, ICD placement was left to discretion of the treating physician—70% of this group received ICDs. Patients were followed up a median of 1.9 years. The primary outcome was a composite of appropriate ICD therapy (n=55) or arrhythmic death (n=10). EPS testing was positive in 39% and negative in 61%. For MTWA results, a “MTWA strategy” was defined whereby patients testing as indeterminate were subsequently judged positive or negative based on the EPS result. These “strategies” had similar positive and negative predictive values for the composite outcome at 1 year—MTWA strategy: PPV 9%, NPV 95%; EPS: PPV 11%, NPV 96%. The results raise a number of issues. First, current evidence does not warrant ICD for primary prevention in patients with ejection fractions of 35%—

40%. Second, predictive values for MTWA reported were not independent of EPS results—those with indeterminate MTWA results were classified according to EPS results. Patients receiving ICDs for primary prevention would, however, not undergo EPS testing. In addition, in the 30% of those MTWA negative not receiving ICDs, the diagnosis of arrhythmic events was likely underestimated due to lack of electrogram recording. Finally, approximately 50% of “appropriate” ICD shocks are unnecessary, as many arrhythmias terminate spontaneously.^[20] While of interest, the study does not inform the questions regarding the clinical utility of MTWA.

- Microvolt T-Wave Alternans Testing for Risk Stratification of Post-MI Patients (MASTER I)^[21] was designed to determine if MTWA predicted life-threatening ventricular tachyarrhythmic events (LTVTE) in MADIT-II type patients (LVEF $\leq 30\%$ post MI) treated with an ICD. Patients were enrolled at 50 centers across the U.S. (n=575); mean age was 65 (SD 11) years, 84% were male, and average follow-up was 2.1 (SD 0.9) years. MTWA results were non-negative in 63% (51% positive and 12% indeterminate)—initially indeterminate tests were repeated. All patients received ICDs. In MTWA non-negative and negative patients LTVTE occurred at annual rates of 6.3% and 5.0%, respectively; a non-negative MTWA result was not significantly associated with LTVTE. Although mean follow-up exceeded 2 years, there were few (n=7, 1.2%) arrhythmic deaths. In contrast, the 2-year sudden cardiac death rate in the MADIT-II ICD arm was 4.9%.^[20] Reasons for this difference are not clear but could reflect improved medical care, better defibrillator technology and programming, or patient selection. Finally, some critique use of LTVTE as an endpoint, as not all will result in SCD if left untreated. However, to alter these results would require differential rates of spontaneous termination in MTWA-negative and MTWA-positive patients—currently no evidence supports that suggestion.
- Leino and colleagues^[22] analyzed heart rate recovery (HRR) in combination with T-wave alternans (TWA) to improve cardiovascular death risk assessment in 1 972 participants of the Finnish Cardiovascular Study (FINCAVAS) with a clinically indicated exercise test. Death certificates were obtained 3 years later to identify all cause and cardiovascular deaths in the cohort. Exercise test variables were compared for survivors and non-survivors. During 48 ± 13 months of follow-up (mean \pm SD), 116 patients died; 55 deaths were cardiovascular. In multivariable Cox analysis after adjustment for common coronary risk factors, high exercise-based TWA ($\geq 60 \mu\text{V}$) and low HRR (≤ 18 bpm) yielded relative risks for all-cause mortality of 5.0 (95% confidence interval 2.1–12.1, $P < .01$) and for cardiovascular mortality of 12.3 (95% confidence interval 4.3–35.3, $P < .01$). High recovery-based TWA ($\geq 60 \mu\text{V}$) and low HRR (≤ 8 bpm) yielded relative risks for all-cause death of 6.1 (95% confidence interval 2.8–13.2, $P < .01$) and for cardiovascular mortality of 8.0 (95% confidence interval 2.9–22.0, $P < .01$).
- Swerdlow et al. measured alternans and nonalternans variability (TWA/V) from electrograms (EGMs) stored in implantable cardioverter-defibrillators before ventricular tachycardia (VT) or fibrillation (VF) in implantable cardioverter-defibrillator patients.^[23] The study goal was to determine whether EGM TWA/V was greater before VT/VF than at baseline. The study reports that EGM TWA/V is greater before spontaneous VT/VF than in control recordings. However, this study is a small case series and it does not examine either ICDs or antiarrhythmic therapy that have relied on the results of T-wave alternans as a patient selection criterion.
- Takasugi et al. evaluated the usefulness of continuous TWA monitoring in ultra-short-term prediction of impending life-threatening ventricular tachyarrhythmia (VTA) upon emergent reperfusion in acute coronary syndrome (ACS) patients.^[24] The study reports that ACS patients at risk of developing VTA soon after reperfusion show warning episodes of increased TWA. However,

this study is a small case series of twenty consecutive ACS patients and it provides very limited evidence on the clinical utility of T-wave alternans in improving patient outcomes.

Clinical Practice Guidelines

American College of Cardiology (ACC)/American Heart Association (AHA)

The current 2008 ACC/AHA practice guidelines for adults with ST-elevation and non-ST-elevation myocardial infarction do not identify T-Wave alternans as a test for the management of patients with ventricular arrhythmias.^[25]

American College of Cardiology (ACC)/American Heart Association (AHA) European Society of Cardiology (ESC)

The 2006 ACC/AHA/European Society of Cardiology (ESC) 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death state that “it is reasonable to use T-wave alternans for improving the diagnosis and risk stratification of patients with ventricular arrhythmias or who are at risk for developing life-threatening ventricular arrhythmias (evidence class IIa; level of evidence A).”^[26] Per the guideline, class IIa evidence is defined as “weight of evidence/opinion is in favor of usefulness/efficacy.” The level of evidence A is defined as “data derived from multiple randomized clinical trials or meta-analyses.” However, the seven publications referenced in support of this recommendation are not randomized controlled trials of t-wave alternans (referenced are six non-randomized studies and one randomized controlled trial of implantable cardio-defibrillator therapy). Therefore, it is not clear how the limited evidence from non-randomized studies supports the class II a, level A designation concerning T-wave alternans.

Summary

There is currently no published evidence from randomized clinical trials (RCTs) that demonstrates the clinical utility, or how patient management was changed, as a result of the T-wave alternans testing. In the absence of such trials, it cannot be determined how use of T-wave alternans testing changes patient management/treatment decisions and impacts health outcomes. Therefore, T-waves alternans testing is considered investigational.

REFERENCES

1. BlueCross BlueShield Association Medical Policy Reference Manual "T-Wave Alternans." Policy No. 2.02.13
2. Moss, AJ, Zareba, W, Hall, WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002 Mar 21;346(12):877-83. PMID: 11907286
3. Moss, AJ, Hall, WJ, Cannom, DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med*. 1996 Dec 26;335(26):1933-40. PMID: 8960472
4. Buxton, AE, Lee, KL, Fisher, JD, Josephson, ME, Prystowsky, EN, Hafley, G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter

- Unsustained Tachycardia Trial Investigators. *N Engl J Med*. 1999 Dec 16;341(25):1882-90. PMID: 10601507
5. TEC Assessment 2005. "Microvolt T-wave alternans testing to risk stratify patients being considered for ICD therapy for primary prevention of sudden death." BlueCross BlueShield Association Technology Evaluation Center, Vol. 20, Tab 9.
 6. TEC Assessment 2006. "Microvolt T-wave alternans testing to risk stratify patients being considered for ICD therapy for primary prevention of sudden death." BlueCross BlueShield Association Technology Evaluation Center, Vol. 21, Tab 14.
 7. Bloomfield, DM, Steinman, RC, Namerow, PB, et al. Microvolt T-wave alternans distinguishes between patients likely and patients not likely to benefit from implanted cardiac defibrillator therapy: a solution to the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II conundrum. *Circulation*. 2004 Oct 5;110(14):1885-9. PMID: 15451804
 8. Hohnloser, SH, Ikeda, T, Bloomfield, DM, Dabbous, OH, Cohen, RJ. T-wave alternans negative coronary patients with low ejection and benefit from defibrillator implantation. *Lancet*. 2003 Jul 12;362(9378):125-6. PMID: 12867114
 9. Chow, T, Kereiakes, DJ, Bartone, C, et al. Prognostic utility of microvolt T-wave alternans in risk stratification of patients with ischemic cardiomyopathy. *J Am Coll Cardiol*. 2006 May 2;47(9):1820-7. PMID: 16682307
 10. Chan, PS, Stein, K, Chow, T, Fendrick, M, Bigger, JT, Vijan, S. Cost-effectiveness of a microvolt T-wave alternans screening strategy for implantable cardioverter-defibrillator placement in the MADIT-II-eligible population. *J Am Coll Cardiol*. 2006 Jul 4;48(1):112-21. PMID: 16814657
 11. Chan, PS, Gold, MR, Nallamothu, BK. Do Beta-blockers impact microvolt T-wave alternans testing in patients at risk for ventricular arrhythmias? A meta-analysis. *J Cardiovasc Electrophysiol*. 2010 Sep;21(9):1009-14. PMID: 20384655
 12. Calo, L, De Santo, T, Nuccio, F, et al. Predictive value of microvolt T-wave alternans for cardiac death or ventricular tachyarrhythmic events in ischemic and nonischemic cardiomyopathy patients: a meta-analysis. *Ann Noninvasive Electrocardiol*. 2011 Oct;16(4):388-402. PMID: 22008495
 13. Merchant, FM, Ikeda, T, Pedretti, RF, et al. Clinical utility of microvolt T-wave alternans testing in identifying patients at high or low risk of sudden cardiac death. *Heart Rhythm*. 2012 Mar 8. PMID: 22406384
 14. Gupta, A, Hoang, DD, Karliner, L, et al. Ability of microvolt T-wave alternans to modify risk assessment of ventricular tachyarrhythmic events: a meta-analysis. *Am Heart J*. 2012 Mar;163(3):354-64. PMID: 22424005
 15. Chen, Z, Shi, Y, Hou, X, Xu, S, Zou, J. Microvolt T-wave alternans for risk stratification of cardiac events in ischemic cardiomyopathy: a meta-analysis. *Int J Cardiol*. 2013 Sep 1;167(5):2061-5. PMID: 22683284
 16. Chow, T, Kereiakes, DJ, Bartone, C, et al. Microvolt T-wave alternans identifies patients with ischemic cardiomyopathy who benefit from implantable cardioverter-defibrillator therapy. *J Am Coll Cardiol*. 2007 Jan 2;49(1):50-8. PMID: 17207722
 17. Gold, MR, Ip, JH, Costantini, O, et al. Role of microvolt T-wave alternans in assessment of arrhythmia vulnerability among patients with heart failure and systolic dysfunction: primary results from the T-wave alternans sudden cardiac death in heart failure trial substudy. *Circulation*. 2008 Nov 11;118(20):2022-8. PMID: 18955671
 18. Salerno-Uriarte, JA, De Ferrari, GM, Klersy, C, et al. Prognostic value of T-wave alternans in patients with heart failure due to nonischemic cardiomyopathy: results of the ALPHA Study. *J Am Coll Cardiol*. 2007 Nov 6;50(19):1896-904. PMID: 17980258

19. Costantini, O, Hohnloser, SH, Kirk, MM, et al. The ABCD (Alternans Before Cardioverter Defibrillator) Trial: strategies using T-wave alternans to improve efficiency of sudden cardiac death prevention. *J Am Coll Cardiol*. 2009 Feb 10;53(6):471-9. PMID: 19195603
20. Greenberg, H, Case, RB, Moss, AJ, Brown, MW, Carroll, ER, Andrews, ML. Analysis of mortality events in the Multicenter Automatic Defibrillator Implantation Trial (MADIT-II). *J Am Coll Cardiol*. 2004 Apr 21;43(8):1459-65. PMID: 15093884
21. Chow, T, Kereiakes, DJ, Onufer, J, et al. Does microvolt T-wave alternans testing predict ventricular tachyarrhythmias in patients with ischemic cardiomyopathy and prophylactic defibrillators? The MASTER (Microvolt T Wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients) trial. *J Am Coll Cardiol*. 2008 Nov 11;52(20):1607-15. PMID: 18992649
22. Leino, J, Minkkinen, M, Nieminen, T, et al. Combined assessment of heart rate recovery and T-wave alternans during routine exercise testing improves prediction of total and cardiovascular mortality: the Finnish Cardiovascular Study. *Heart Rhythm*. 2009 Dec;6(12):1765-71. PMID: 19959127
23. Swerdlow, C, Chow, T, Das, M, et al. Intracardiac electrogram T-wave alternans/variability increases before spontaneous ventricular tachyarrhythmias in implantable cardioverter-defibrillator patients: a prospective, multi-center study. *Circulation*. 2011 Mar 15;123(10):1052-60. PMID: 21357826
24. Takasugi, N, Kubota, T, Nishigaki, K, et al. Continuous T-wave alternans monitoring to predict impending life-threatening cardiac arrhythmias during emergent coronary reperfusion therapy in patients with acute coronary syndrome. *Europace*. 2011 May;13(5):708-15. PMID: 21317426
25. Krumholz, HM, Anderson, JL, Bachelder, BL, et al. ACC/AHA 2008 performance measures for adults with ST-elevation and non-ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to develop performance measures for ST-elevation and non-ST-elevation myocardial infarction): developed in collaboration with the American Academy of Family Physicians and the American College of Emergency Physicians: endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, Society for Cardiovascular Angiography and Interventions, and Society of Hospital Medicine. *Circulation*. 2008 Dec 9;118(24):2596-648. PMID: 19001027
26. American College of Cardiology(ACC)/American Heart Association(AHA)/European Society of Cardiology(ESC) 2006 Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. [cited 05/20/2014]; Available from: <http://circ.ahajournals.org/content/114/10/e385.full.pdf>

CROSS REFERENCES

[Signal Averaged ECG \(SAECG\)](#), Medicine, Policy No. 21

CODES	NUMBER	DESCRIPTION
CPT	93025	Microvolt T-wave alternans for assessment of ventricular arrhythmias
HCPCS	None	