Aetna considers microvolt T-wave alternans (MTWA) diagnostic testing using the spectral analytic method medically necessary for the evaluation of persons at risk of sudden cardiac death who meet criteria for implantable cardioverter-defibrillator placement.

Aetna considers MTWA diagnostic testing using the spectral analytic method experimental and investigational for all other indications including the following (not an all-inclusive list):

- Diagnosis and risk assessment of acute coronary syndrome
- Evaluation of the adequacy of medical therapy
- Guidance of anti-arrhythmic therapy
- Judgement of the severity of ischemic cardiomyopathy
- Prognosis of pulmonary arterial hypertension
- Risk stratification of cardiac events (e.g., sudden cardiac death) in members following repair of tetralogy of Fallot
- Risk stratification in Brugada syndrome
- Tracking changes in risk during cardiac disease progression

See CPB 0585 - Cardioverter-Defibrillators (../500_599/0585.html).
Background
The term alternans applies to conditions characterized by the sudden appearance of a periodic beat-to-beat change in some aspect of cardiac electrical or mechanical behavior. Many different examples of electrical alternans have been described clinically; a number of others have been reported in the laboratory.

T-wave alternans has long been recognized as a marker of electrical instability in acute ischemia, where it may precede ventricular tachyarrhythmia. Studies have shown that T wave (or ST-T) alternans can also precede non-ischemic ventricular tachyarrhythmias. Considerable interest has recently been shown in the detection of microvolt T wave alternans as a noninvasive marker of the risk of ventricular tachyarrhythmia in patients with chronic heart disease.

Assessment of left ventricular ejection fraction (LVEF), Holter monitoring, and signal-averaged late potentials are the principal non-invasive means of determining the risk of ventricular arrhythmias after myocardial infarction (MI). However, these measures of vulnerability to arrhythmias have been found to be less predictive of arrhythmic events than invasive electrophysiologic testing.

Microvolt T-wave alternans testing is performed by placing high-resolution electrodes, designed to reduce electrical interference, on a patient’s chest prior to a period of controlled exercise (CMS, 2005). These electrodes detect tiny beat-to-beat changes, on the order of one-millionth of volt, in the electrocardiogram (EKG) T-wave. Spectral analysis is used to calculate these minute voltage changes. Spectral analysis is a sensitive mathematical method of measuring and comparing time and the electrocardiogram signals. Software then analyzes these microvolt changes and produces a report to be interpreted by a physician.

T-wave alternans has primarily been used for defining the risk of ventricular arrhythmias in persons at risk for sudden cardiac death and determining which patients are most likely to benefit.
from implantable cardioverter-defibrillators. Cambridge Heart, Inc. (Fort Lauderdale, FL) Cardiac Diagnostic System Model CH 2000, which measures T-wave alternans at rest and with exercise, was cleared by the Food and Drug Administration (FDA) based on an 510(k) application.

A decision memorandum from the Centers for Medicare and Medicaid Services (CMS, 2006) found that the quality of evidence is adequate to conclude that microvolt T-wave alternans testing using a spectral analysis algorithm can improve net health outcomes, and is reasonable and necessary for Medicare patients who are candidates for implantable cardioverter defibrillator (ICD) placement. The decision memorandum explained that the reviewed literature contains a number of studies evaluating the use of microvolt T-wave alternans (MTWA) in a variety of population settings, including subjects with congestive heart failure (CHF), ischemic CHF, non-ischemic CHF, dilated cardiomyopathy, hypertrophic cardiomyopathy, post-MI, and in healthy subjects. The decision memorandum noted that the material reviewed included not only small prospective studies with a homogenous patient population, but also large systematic reviews with heterogeneous patient populations. Also included in the CMS analysis were studies that looked specifically at MTWA's role as a risk stratification tool in patient populations similar to those in pivotal clinical studies of implantable cardioverter-defibrillators.

The decision memorandum noted that most of the studies used in CMS’ assessment of MTWA included measures of diagnostic accuracy (e.g., sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (CMS, 2006). CMS found that, when reviewing these measures of accuracy, MTWA testing demonstrated superior findings related to sensitivity and NPV when compared to other diagnostic tests used to assess risk of ventricular tachyarrhythmias.

The CMS decision memorandum stated that “[a]cross a number of population settings, MTWA [microvolt T-wave alternans] consistently demonstrates superiority when compared to other diagnostic measures that assess risk of VTEs [ventricular
 Though some of the studies noted some limitations related to methodology as well as research design, these limitations were not enough to invalidate their findings” (CMS, 2006).

The CMS decision memorandum commented on a technology assessment of MTWA published by the BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC). The TEC assessment concluded that the available evidence on MTWA is insufficient to permit conclusions regarding the effect on health outcomes. Regarding use of MTWA in evaluating subjects eligible for placement of an implantable cardioverter defibrillator given current patient selection criteria, the TEC assessment stated that the available evidence is limited (BCBSA, 2005).

The CMS decision memorandum explained that differences in the conclusions of the TEC assessment and CMS analysis are due, in part, to the unique characteristics of the Medicare-eligible population (i.e. elderly, and more likely to have multiple co-morbidities) (CMS, 2006). The decision memorandum explained that sudden cardiac death has a higher potential to occur as a result of ventricular tachyarrhythmias in this population. The decision memorandum explained that potential harms from adverse events are also more likely to occur within this population. The CMS decision memorandum stated that “because of these features of the Medicare population, the potential for benefit or harm from ICD placement varies from that of the BCBSA population at large, and plays a prominent role in our decision making.” The decision memorandum also noted that indications for ICD placement also differ between the 2 organizations. “Because of the higher potential for VTE occurrence in the Medicare population, and because CMS recognizes VTEs as an indication for ICD placement, CMS feels that the use of MTWA is reasonable and necessary to address problems related to VTE and its adverse consequences.”

The CMS decision memorandum concluded that MTWA is a useful risk stratification tool and can identify which heart patients are at negligible risk of sudden death, and who may therefore be able to
avoid implantable cardioverter defibrillator placement and its attendant risks (CMS, 2006).

The CMS decision memorandum states that MTWA testing is only covered when the spectral analytic method is used (CMS, 2006) because the evidence only supports the use of this algorithm for the detection of MTWA. The decision memorandum explained that, although algorithms other than spectral analysis have been used to measure MTWA (e.g., modified moving average), CMS identified no peer-reviewed published articles discussing these other algorithms.

It has also been suggested that MTWA testing may be useful in determining the types and doses of medications (e.g., angiotensin converting enzyme inhibitors, beta-blockers, aldosterone antagonists) used to treat underlying cardiac conditions (e.g., left ventricular dysfunction, patients with recent MI) and to suppress arrhythmias. However, there are no prospective clinical studies of the use of MTWA testing in adjusting pharmacotherapy.

Verrier and Nieminen (2010) stated that over 100 studies enrolling a total of more than 12,000 patients support the predictivity of TWA testing for cardiovascular mortality and sudden cardiac death during both exercise and ambulatory electrocardiogram monitoring. To date, the main intended application has been to aid decision-making for cardioverter-defibrillator implantation. The prospect that TWA could be used to guide pharmacologic therapy has not received adequate attention. These investigators reviewed the literature supporting the utility of TWA as a therapeutic marker of anti-arrhythmic effects and pro-arrhythmia for each of the major anti-arrhythmic drug classes. Beta-adrenergic and sodium channel blocking agents are the most widely studied drug classes in clinical TWA investigations, which report reductions in TWA magnitude. Patients with Brugada syndrome constitute a significant exception, because sodium channel blockade provokes the diagnostic electrocardiogram changes as well as macroscopic TWA. Calcium channel blockers have undergone extensive research in several animal models, but, surprisingly, no clinical studies on TWA with this class of drugs have been performed.
Interestingly, TWA may help to detect the beneficial effects of non-antiarrhythmic agents such as the angiotensin II receptor blocker valsartan, which exert their protective effects through putative indirect actions on myocardial remodeling. There is also suggestive evidence that the pro-arrhythmic effects associated with cardiovascular and non-cardiovascular agents may be disclosed by elevated levels of TWA. Thus, the emerging collective evidence indicates the broad utility of TWA in estimating anti-arrhythmic and pro-arrhythmic effects of diverse agents across differing pathologies. The authors concluded that quantitative analysis of TWA has considerable potential to guide pharmacologic therapy.

Gold et al (2008) noted that sudden cardiac death remains a leading cause of mortality despite advances in medical treatment for the prevention of ischemic heart disease and heart failure. Recent studies showed a benefit of implantable cardioverter-defibrillator implantation, but appropriate shocks for ventricular tachyarrhythmias were noted only in a minority of patients during 4 to 5 years of follow-up. Accordingly, better risk stratification is needed to optimize patient selection. In this regard, MTWA has emerged as a potentially useful measure of arrhythmia vulnerability, but it has not been evaluated previously in a prospective, randomized trial of implantable cardioverter-defibrillator therapy. This investigation was a prospective substudy of the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) that included 490 patients at 37 clinical sites. Microvolt T-wave alternans tests were classified by blinded readers as positive (37 %), negative (22 %), or indeterminate (41 %) by standard criteria. The composite primary end point was the first occurrence of any of the following events: (i) sudden cardiac death, (ii) sustained ventricular tachycardia/fibrillation, or (iii) 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 % confidence interval [CI]: 0.60 to 2.59, p = 0.56) or MTWA-negative and non-negative (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 MTWA-negative patients can not be excluded given the sample size of this study. Accordingly, these results suggested that MTWA is not useful as an aid in clinical decision making on implantable cardioverter-defibrillator therapy among patients with heart failure and left ventricular systolic dysfunction.

Scirica (2010) stated that although there are many established tools for diagnosis, prognosis, and clinical decision making for acute coronary syndrome, understanding the advantages and limitations of each tool according the clinical scenario is essential. Several emerging tools, such as novel biomarkers (e.g., high-sensitivity troponin and growth differential factor-15), electroencephalographic (ECG) techniques (e.g., heart rate turbulence or TWA), and imaging modalities (computed tomography angiography and cardiac magnetic resonance) may potentially improve clinical care; however, they must be fully evaluated and validated in different scenarios and patient cohorts before they are incorporated into clinical practice.

On behalf of the International Society for Holter and Noninvasive Electrocardiology (and co-sponsored by the Japanese Circulation Society, the Computers in Cardiology Working Group on e-Cardiology of the European Society of Cardiology, and the European Cardiac Arrhythmia Society), Verrier et al (2011) prepared a consensus guideline on the electrocardiographic phenomenon of TWA. This statement focused on its physiological basis and measurement technologies and its clinical utility in stratifying risk for life-threatening ventricular arrhythmias. Signal processing techniques including the frequency-domain spectral method and the time-domain modified moving average method have demonstrated the utility of TWA in arrhythmia risk stratification in prospective studies in more than 12,000 patients. The majority of exercise-based studies using both methods have reported high relative risks for cardiovascular mortality and for sudden cardiac death in patients with preserved as well as depressed LVEF. Studies with ambulatory electrocardiogram-based TWA analysis with modified moving
average method have yielded significant predictive capacity. However, negative studies with the spectral method have also appeared, including 2 interventional studies in patients with implantable defibrillators. Meta-analyses have been performed to gain insights into this issue. Frontiers of TWA research include use in arrhythmia risk stratification of individuals with preserved ejection fraction, improvements in predictivity with quantitative analysis, and utility in guiding medical as well as device-based therapy. The authors concluded that although TWA appears to be a useful marker of risk for arrhythmic and cardiovascular death, there is as yet no definitive evidence from interventional trials that it can guide therapy.

In a meta-analysis, Chen et al (2013) systematically reviewed current literature to determine the ability of MTWA to predict the outcome severity following ischemic cardiomyopathy (ICM). Major endpoints include composite endpoint of cardiac mortality and severe arrhythmic events in primary prevention of patients with ICM, as well as all-cause mortality (cardiac death, and/or non-cardiac death). A total of 7 trials were included by using MTWA for risk stratification of cardiac events in 3,385 patients with ICM. All patients were distributed into two groups according to the results of MTWA tests: non-negative group included positive and indeterminate, and negative group. Compared with the negative group, non-negative group showed increased rates of cardiac mortality or severe arrhythmic events (RR = 1.65, 95% CI: 1.32 to 2.071), sudden cardiac death (SCD) (RR = 2.04 95% CI: 1.11 to 3.75), and all-cause mortality (RR = 2.11, 95% CI: 1.60 to 2.79). The funnel plot revealed that there might be bias within current publications. The fail-safe number of composite endpoint and all-cause mortality was 14.42 and 18.93, respectively (when p = 0.01). The fail-safe number of SCD was 1.07 (when p = 0.05), which may be caused by the small case number of included studies and some patients with ICD included. The authors concluded that the non-negative group of MTWA had a nearly double risk of severe outcomes compared with the negative group. Therefore, MTWA represents a potential useful tool for judging the severity of ICM.

Quan and associates (2014) stated that exercise-based spectral
TWA has been proposed as a non-invasive tool for identifying patients at risk of SCD and cardiac mortality. Prior studies have indicated that ambulatory electrocardiogram (AECG)-based TWA is an important alternative platform to exercise for risk stratification of cardiac events. These investigators reviewed data regarding 24-hour AECG-based TWA and discussed its potential role in risk stratification of fatal cardiac events across a series of patient risk profiles. Prospective clinical studies of the predictive value of AECG-based TWA obtained with daily activity published between January 1990 and November 2014 were retrieved. Major end-points included composite end-point of SCD, cardiac mortality, and severe arrhythmic events. Data were accumulated from 5 studies involving a total of 1,588 patients, including 317 positive and 1,271 negative TWA results. Compared with the negative group, positive group showed increased rates of SCD (hazard ratio [HR]: 7.49, 95 % CI: 2.65 to 21.15), cardiac mortality (HR: 4.75, 95 % CI: 0.42 to 53.55), and composite end-point (SCD, cardiac mortality, and severe arrhythmic events, HR: 5.94, 95 % CI: 1.80 to 19.63). For the 4 studies evaluating TWA measured using the modified moving average method, the HR associated with a positive versus negative TWA result was 9.51 (95 % CI: 4.99 to 18.11) for the composite end-point. The authors concluded that the positive group of AECG-based TWA has a nearly 6-fold risk of severe outcomes compared with the negative group. Therefore, AECG-based TWA provided an accurate means of predicting fatal cardiac events.

Goldberger and colleagues (2014) performed a meta-analysis to estimate the performance of 12 commonly reported risk stratification tests as predictors of arrhythmic events in patients with non-ischemic dilated cardiomyopathy. A total of 45 studies enrolling 6,088 patients evaluating the association between arrhythmic events and predictive tests (baroreflex sensitivity, heart rate turbulence, heart rate variability, left ventricular end-diastolic dimension, LVEF, electrophysiology study, non-sustained ventricular tachycardia, left bundle branch block, signal-averaged electrocardiogram, fragmented QRS, QRS-T angle, and TWA) were included. Raw event rates were extracted, and meta-analysis was performed using mixed effects methodology. They also used the trim-and-fill method to estimate the influence of missing studies
on the results. Patients were 52.8 ± 14.5 years of age, and 77% were male; LVEF was 30.6 ± 11.4%. Test sensitivities ranged from 28.8% to 91.0%, specificities from 36.2% to 87.1%, and odds ratios (OR) from 1.5 to 6.7. Odds ratio was highest for fragmented QRS and TWA (OR: 6.73 and 4.66, 95% CI: 3.85 to 11.76 and 2.55 to 8.53, respectively) and lowest for QRS duration (OR: 1.51, 95% CI: 1.13 to 2.01). None of the autonomic tests (heart rate variability, heart rate turbulence, baroreflex sensitivity) was significant predictors of arrhythmic outcomes. Accounting for publication bias reduced the OR for the various predictors but did not eliminate the predictive association. The authors concluded that techniques incorporating functional parameters, depolarization abnormalities, repolarization abnormalities, and arrhythmic markers provided only modest risk stratification for SCD in patients with non-ischemic dilated cardiomyopathy. It is likely that combinations of tests will be needed to optimize risk stratification in this population.

An UpToDate review on “T wave (repolarization) alternans: Clinical aspects” (Narayan, 2015) states that “Major society guidelines -- The major limitation to implementation of TWA protocols is that specific guidance is not available on how to use TWA in clinical practice. In addition, the optimum measurement conditions and criteria for detecting TWA remain controversial. We agree with the 2008 American Heart Association/American College of Cardiology/Heart Rhythm Society (AHA/ACC/HRS) scientific statement on noninvasive risk stratification, which concluded that a moderate amount of data suggest that TWA may be useful for risk stratification for SCD, but that further information will be needed to determine the clinical applicability of this test”.

Risk Stratification of Sudden Cardiac Death following Repair of Tetralogy of Fallot:

Cheung et al (2002) stated that sustained MTWA is a marker of increased risk for malignant ventricular arrhythmia (VA). There is a significant risk of arrhythmia and sudden death after repair of congenital heart disease. These researchers determined the prevalence and characteristics of TWA after repair of tetralogy of
Fallot (TOF). T-wave alternans was evaluated during bicycle exercise in 49 subjects who had consecutively undergone transatrial-transpulmonary repair. Median values for age, age at repair, and follow-up duration were 14.9 years (11.5 to 20.8), 1.6 years (0.2 to 4.9), and 11.6 years (9.4 to 17.2), respectively. All patients were in New York Heart Association (NYHA) functional class I and were asymptomatic. Median QRS duration was 120 msec (80 to 150). Sustained TWA was detected in 7 (23%) of 31 subjects with adequate tests. In these 7 subjects, median onset heart rate (HR) was 120 (98 to 155). Median HR threshold as a percentage of predicted maximum HR (220 – age) was 58% (48 to 77). Sustained TWA prevalence was not significantly different compared with normal subjects (7/31 versus 9/83; p = 0.1). Onset HR in the TOF group was significantly lower [mean (SD) of 122 (20) versus 139 (12), p < 0.05]. In the TOF group with sustained TWA, the TWA occurred in 4 of 7 at less than 60% predicted maximum HR versus 1 of 9 normal subjects (p < 0.05); 3 of 7 had onset HR less than 120 versus 0 of 9 normal subjects (p < 0.03). There was no significant difference in age, gender, transannular patch use, restrictive right ventricular physiology, QRS duration, QTc, QT/QRS dispersion, or non-sustained ventricular tachycardia in subjects with or those without sustained TWA. The authors concluded that the onset HR for sustained TWA was significantly lower after repair of TOF. They stated that further study is needed to examine if this represents an increased risk for arrhythmia in this patient group.

Bartczak et al (2015) noted that indications for SCD primary prevention are unknown in patients with repaired ToF. The role of MTWA in SCD risk stratification was documented. However, the prevalence of spectral MTWA and its association with VA in adults after ToF repair were not elucidated. In this study, MTWA, ECG, ambulatory ECG monitoring, echocardiography, and spiroergometry were evaluated in 102 adults after ToF repair. Microvolt T-wave alternans results were classified as normal: negative(−), abnormal: positive(+), and indeterminate(ind). Owing to similar prognostic significance, MTWA(+) and MTWA(ind) due to patient factors were combined into non-negative group: MTWA(abnormal). Microvolt T-wave alternans(abnormal) was more frequent in the studied group as compared with controls (p
The MTWA(abnormal) group had greater right ventricular end-diastolic diameter (p = 0.005), higher incidence of pulmonary regurgitation (p = 0.015), lower peak oxygen consumption (p = 0.01), and higher VE/VCO2 slope (p = 0.04) in comparison with MTWA(normal). Univariate logistic regression proved pulmonary regurgitation (OR = 3.57, 95 % CI: 1.27 to 10.04), VA (OR = 3.26, 95 % CI: 1.06 to 10.05), right ventricular end-diastolic enlargement (OR = 1.11, 95 % CI: 1.03 to 1.2), increase in VE/VCO2 slope (OR = 1.08, 95 % CI: 1.01 to 1.17), and decrease in peak oxygen uptake (OR = 0.91, 95 % CI: 0.83 to 0.99) to increase MTWA(abnormal) prevalence. The authors concluded that in adults after ToF repair, abnormal MTWA occurred more often than in controls. Probability of abnormal MTWA did not rise with prevalence of malignant VA; however, presence of abnormal MTWA was associated with VA risk factors: pulmonary regurgitation, right ventricular enlargement, and consequent heart failure. They stated that the role of MTWA in selecting patients late after ToF repair at risk of SCD needs further observation.

Furthermore, UpToDate reviews on “Pathophysiology, clinical features, and diagnosis of tetralogy of Fallot” (Doyle and Kavanaugh-McHugh, 2015) and “Management and outcome of tetralogy of Fallot” (Doyle et al, 2015) do not mention the use of MTWA as a diagnostic/management tool.

Prognosis of Pulmonary Arterial Hypertension:

Danilowicz-Szymanowicz et al (2016) stated that MTWA is a well-examined parameter for the risk stratification of SCD in patients with left ventricular dysfunction (LVD). However, the role of MTWA in pulmonary arterial hypertension (PAH) remains obscure. These researchers analyzed the profile of MTWA among PAH patients in comparison with LVD patients and healthy volunteers. The prospectively study included 22 patients with PAH (mean pulmonary artery pressure greater than or equal to 25 mm Hg and pulmonary capillary wedge pressure less than or equal to 15 mm Hg during right heart catheterization; mean age of 40 ± 17 years); 24 with LVD [LVEF less than or equal to 35 %; mean age of 40 ± 11 years]; and 28 healthy volunteers (mean age...
of 41 ± 8 years). Patients with persistent atrial arrhythmia were excluded. The MTWA (spectral method) categories were positive, negative, or indeterminate (MTWA_pos, MTWA_neg, or MTWA_ind, respectively). MTWA_pos and MTWA_ind were qualified as abnormal (MTWA_abn). Statistical analyses (Mann-Whitney U, chi-square with Yates's correction, Fisher’s exact test) were performed. Patients with PAH had higher LVEF than LVD patients (61 ± 7 % versus 27 ± 7 %; p < 0.05); MTWA_abn was observed more frequently in the PAH and LVD groups than in the healthy volunteers. Patients with PAH were characterized by a considerable percentage of MTWA_pos and MTWA_abn (59 % and 73 %, respectively), but this did not differ from LVD patients. The authors concluded that patients with PAH are characterized by a high rate of MTWA abnormalities similar to LVD patients, despite the relevant differences in LVEF. Moreover, they stated that further research is needed to elucidate the clinical significance and prognostic value of this data, particularly in the context of SCD underlying mechanisms in PAH patients.

Evaluation of the Adequacy of Medical Therapy/Guidance of ICD implantation/Tracking Changes in Risk during Cardiac Disease Progression:

Verrier and Sroubek (2016) addressed current questions regarding use of TWA to stratify risk for SCD. Both of the currently available commercial methodologies, namely, the frequency-domain spectral method and the time-domain modified moving average (MMA) method, are supported by guideline statements, cleared by the FDA, and covered by the CMS. Similar numbers of patients have been enrolled in predictive studies; OR generated by the 2 methods are similar including in a head-to-head study. However, in 2 prospective studies, prediction by TWA with the spectral method was negative, likely due to withdrawal of beta-blockade before the test with later resumption, while all studies with MMA have achieved prediction when the commercial software was used appropriately. The authors noted that questions currently undergoing investigation include TWA’s potential to (i) guide ICD implantation, (ii) track changes in risk during cardiac disease progression, and (iii) evaluate the adequacy of medical therapy.
Barbosa and colleagues (2016) stated that Chagas disease (ChD) may lead to life-threatening heart disease, including malignant ventricular arrhythmias. The use of ICDs has become the main therapeutic strategy for secondary prevention of SCD in ChD. Microvolt T-wave alternans is a direct measure of ventricular repolarization instability and has emerged as a potentially useful way of determining arrhythmia vulnerability. However, this methodology has not been evaluated in patients with ChD. In a prospective study, these researchers evaluated the predictive value of MTWA testing for appropriate therapy or death in ChD patients with ICDs. This study included consecutive patients who received ICD implantations in a Brazilian tertiary referral center. A total of 72 patients were followed for a median time of 422 (range of 294 to 642) days; 33 patients had ChD. The MTWA was non-negative (positive or indeterminate) in 27 (81.8 %) of ChD patients. The combined primary outcome (appropriate ICD therapy or death) occurred in 29 patients (40.3 %); 17 out 33 ChD patients presented the primary outcome. There was a statistically significant difference in event-free survival between ChD patients with negative and non-negative MTWA results (p = 0.02). Non-negative MTWA tests nearly triple the risk of appropriate ICD therapy or death (HR = 2.7, 95 % CI: 1.7 to 4.4, p = 0.01) in patients with ChD and was the only variable associated with outcomes. The sensitivity and the NPV was 100 % in ChD patients. The authors concluded that MTWA may be useful in recognizing high-risk ICD patients who may require adjunctive therapies with anti-arrhythmic drugs or catheter ablation.

Risk Stratification in Brugada Syndrome:

Adler and colleagues (2016) noted that risk stratification in Brugada syndrome remains a clinical challenge because the event rate is low but the presenting symptom is often cardiac arrest (CA). These investigators reviewed the data on risk stratification. A history of CA or malignant syncope is a strong predictor of spontaneous ventricular fibrillation (VF), whereas the prognostic value of a history of familial sudden death and the presence of a
SCN5A mutation are less well defined. On the EKG, the presence of spontaneous type I electrocardiogram increases the risk for VF in all studies, whereas the presence of fragmented QRS complexes and early repolarization correlates with increased risk in several studies. The authors concluded that signal-averaged techniques using late potentials and MTWA showed some promising results in small studies that need to be confirmed. The value of electrophysiological studies for predicting spontaneous VF remains controversial, and this included programmed stimulation protocols that avoid a third extra-stimuli or stimulation from the right ventricular outflow. Risk prediction is particularly challenging in children and women.

Sakamoto and associates (2017) stated that the prognostic value of the seasonal variations of TWA and heart rate variability (HRV), and the seasonal distribution of VF in Brugada syndrome (Br-S) is unknown. These researchers assessed the utility of seasonal variations in TWA and HRV for risk stratification in Br-S using a 24-h multi-channel Holter EKG (24-M-EKG). They enrolled 81 patients with Br-S (grouped according to their history of VF, n = 12; syncope, n = 8; no symptoms, n = 61) who underwent 24- M-EKG in all 4 seasons. Precordial electrodes were attached to the 3rd (3L-V2) and 4rth (4L-V2, 4L-V5) intercostal spaces. These investigators determined the maximum TWA (max-TWA) values and calculated HRV during night and morning time periods for all seasons. During a follow-up period of 5.8 ± 2.8 years, 11 patients experienced new VF episodes and there was a peak in new VF episodes in the summer. The VF group had the greatest 3L-V2 max-TWA value during morning time in the summer among the 3 groups and showed higher 3L-V2 max-TWA value than in the other seasons. The cut-off value for the 3L-V2 max-TWA during morning time in the summer was determined to be 42 μV using ROC analysis (82 % sensitivity, 74 % specificity; p = 0.0006). The authors concluded that multi-variate analysis revealed that a 3L-V2 max-TWA value of greater than or equal to 42 μV during morning time in the summer and previous VF episodes were predictors of future VF episodes. They stated that the 3L-V2 max-TWA value during morning time in the summer may be a useful predictor of future VF episodes in Br-S.
Furthermore, an UpToDate review on “Brugada syndrome: Clinical presentation, diagnosis, and evaluation” (Wylie and Garlitski, 2017) does not mention T-wave alternans as a means of risk stratification.

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<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<td>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</td>
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<td>CPT codes covered if selection criteria are met:</td>
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**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

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<td>I27.0</td>
<td>Primary pulmonary hypertension</td>
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<td>I48.0 - I48.1, I49.1, I49.40 - I49.9</td>
<td>Other cardiac arrhythmias [other than tachycardia, ventricular fibrillation, ventricular flutter, and cardiac arrest]</td>
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<td>Q21.3</td>
<td>Tetralogy of Fallot [not covered for risk stratification of cardiac events e.g., sudden cardiac death]</td>
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<tr>
<td>R00.1</td>
<td>Bradycardia, unspecified</td>
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The above policy is based on the following references:


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28. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Microvolt T-wave alternans testing to risk stratify patients being considered for ICD therapy for


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Amendment to
Aetna Clinical Policy Bulletin Number: 0579 T-Wave Alternans

There are no amendments for Medicaid.