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Risk Stratification Tests for Determining Arrhythmias (Signal-Averaged Electrocardiography [SAECG] and Microvolt T-Wave Alternans [MTWA])

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Related Policies (if applicable)
None

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Coverage

Microvolt T-wave alternans (MTWA) as a technique of risk stratification for primary or secondary prevention of fatal arrhythmias and sudden cardiac death (SCD) **may be considered medically necessary** in patients who are at risk for developing life-threatening ventricular arrhythmias (e.g., known cardiac dysrhythmias, history of myocardial infarction [MI], congestive heart failure, or cardiomyopathy).

MTWA testing **is considered experimental, investigational, and/or unproven** for all other indications.

Signal-averaged electrocardiography (SAECG), as a technique of risk stratification for arrhythmias after prior MI, **is considered not medically necessary**.

Other applications of SAECG **are considered experimental, investigational and/or unproven,** including but not limited to the following:

- Use in patients with cardiomyopathy,
- Use in patients with syncope,
- Assessment of success after surgery for arrhythmia,
- Detection of acute rejection of heart transplants,
- Assessment of efficacy of antiarrhythmic drug therapy, or
- Assessment of success of pharmacological, mechanical, or surgical interventions to restore coronary artery blood flow.

Policy Guidelines

None.

Description

Signal-averaged electrocardiography and microvolt T-wave alternans have been investigated as techniques of risk stratification for arrhythmic events in patients with a variety of cardiac conditions, including history of myocardial infarction (MI), congestive heart failure, or cardiomyopathy. Patients with these disorders at high-risk of sudden cardiac death (SCD), may be treated with drugs to suppress the emergence of arrhythmias or may undergo implantation of cardiac defibrillators to terminate tachyarrhythmias when they occur. Because SCD, whether from arrhythmias or pump failure, is one of the most common causes of death after a MI or in patients with dilated cardiomyopathy, there is substantial interest in risk stratification to target therapy.

Microvolt T-Wave Alternans (MTWA)

MTWA refers to a beat-to-beat variability in T-wave amplitude. Because a routine electrocardiogram (EKG) cannot detect these small fluctuations, this test requires specialized sensors to detect the fluctuations and computer algorithms to evaluate the results. T-wave alternans is measured by a provocative test that requires gradual elevation of the heart rate to more than 110 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 (SDs) by which the peak signal of the T-wave exceeds the background noise. This 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 other values are indeterminate.

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

Signal-Averaged Electrocardiography (SAECG)

SAECG is a technique involving computerized analysis of small segments of a standard EKG to detect abnormalities, termed ventricular late potentials (VLPs), that would be otherwise obscured by "background" skeletal muscle activity. VLPs reflect aberrant, asynchronous electrical impulses arising from viable isolated cardiac muscle bordering an infarcted area and are thought to be responsible for ventricular tachyarrhythmias.

Regulatory Status
There are several devices and processing software that have received U.S. Food and Drug Administration (FDA) 510(k) clearance for the recording and measurement of MTWA. As far as devices for SAECG, numerous ECG devices are equipped with enhanced technology that allows signal averaging.

Rationale

This medical policy has been updated periodically with searches of the PubMed database. Following is a summary of the key literature to date.

Medical policies assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these policies, and credible information on technical reliability is available from other sources.

Microvolt T-Wave Alternans (MTWA)
Primary prevention implantable cardioverter-defibrillators (ICD) trials (e.g., MADIT-II and SCD-HeFT) have changed the perspective on selection and risk stratification for use of ICDs. (1) In the MADIT-II trial, implantable defibrillators were shown to be effective in patients selected on the basis of prior myocardial infarction (MI) and reduced ejection fraction; SCD-HeFT inclusion criteria required reduced ejection fraction, but not previous MI. Prior studies of implantable defibrillators had selected patients using results of electrophysiologic testing and symptoms. (2, 3) Given results from these trials, it is critical whether any additional risk stratification tool(s) can identify with sufficient accuracy patients who might or might not benefit from ICD implantation. For example, can T-wave alternans testing identify patients who would otherwise be appropriate for an ICD based in trial inclusion criteria, but who would actually not benefit from an ICD? The rationale for T-wave alternans testing is primarily that patients with a negative result will not benefit from an ICD. Evidence from prospective cohort studies can accurately define the predictive ability of MTWA for sudden cardiac death. This evidence on risk

may impact clinical management, if there are well-defined levels of risk that are linked to different management strategies.

Literature Review

Verrier and Nieminen (2010) states that over 100 studies enrolling a total of more than 12,000 patients support the predictivity of T-wave alternans (TWA) testing for cardiovascular mortality and sudden cardiac death during both exercise and ambulatory electrocardiogram monitoring. (4) 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. The literature supporting the utility of TWA as a therapeutic marker of antiarrhythmic effects and proarrhythmia is reviewed for each of the major antiarrhythmic 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 proarrhythmic 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 antiarrhythmic and proarrhythmic effects of diverse agents across differing pathologies. The authors concluded that quantitative analysis of TWA has considerable potential to guide pharmacologic therapy.

Verrier et al. (2011) prepared a consensus guideline on behalf of the International Society for Holter and Noninvasive Electrocardiology. (5) The guideline discussed the electrocardiographic phenomenon of T-wave alternans (TWA) (i.e., a beat-to-beat alternation in the morphology and amplitude of the ST-segment or T-wave), with a focus on its physiological basis and measurement technologies and its clinical utility in stratifying risk for life-threatening ventricular arrhythmias. Overall, the authors concluded that it is reasonable to consider MTWA evaluation whenever there is suspicion of vulnerability to lethal cardiac arrhythmias. However, there is as yet no definitive evidence from interventional trials that it can guide therapy.

In 2013, Chen et al. systematically reviewed current literature and carried out a meta-analysis to determine the ability of MTWA to predict the outcome severity after ischemic cardiomyopathy (ICM). (6) 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). Seven trials were included by using MTWA for risk stratification of cardiac events in 3385 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%CrI=1.32, 2.071), SCD (RR=2.04 95%CrI=1.11, 3.75), and all-cause mortality (RR=2.11, 95%CrI=1.60, 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. Reviewers 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 et al. (2014) reviewed data regarding 24-hour ambulatory electrocardiogram (AECG)-based MTWA and its potential role in risk stratification of fatal cardiac events across a series of patient risk profiles. (7) 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% confidence interval [CI]: 2.65 to 21.15), cardiac mortality (HR: 4.75, 95% CI: 0.42 to 53.55), and composite endpoint (sudden cardiac death [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 endpoint. The positive group of AECG-based TWA had a nearly six-fold risk of severe outcomes compared with the negative group. Therefore, AECG-based TWA provides an accurate means of predicting fatal cardiac events.

While MTWA is a well-examined parameter for the risk stratification of SCD in patients with left ventricular dysfunction (LVD), the role of MTWA in pulmonary arterial hypertension (PAH) remains obscure. In 2016, Danilowicz-Szymanowicz et al. aimed to analyze the profile of MTWA among PAH patients in comparison with LVD patients and healthy volunteers. (8) The prospectively study included 22 patients with PAH (mean pulmonary artery pressure ≥ 25 mm Hg and pulmonary capillary wedge pressure ≤15 mm Hg during right heart catheterization; mean age, 40±17 years); 24 with LVD [left ventricular ejection fraction (LVEF) ≤35%; mean age, 40±11 years]; and 28 healthy volunteers (mean age, 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. PAH patients had higher LVEF than LVD patients (61±7% vs. 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. Further research is required to elucidate the clinical significance and prognostic value of this data, particularly in the context of SCD-underlying mechanisms in PAH patients.

Karpuz et al. (2017) evaluated the predictive value of myocardial performance on arrhythmia and mortality via tissue-Doppler and microvolt T-wave alternans in infants with hypoxic-ischemic encephalopathy treated with therapeutic hypothermia-rewarming. (9) The study included 23 term newborns having criteria for hypoxic-ischemic encephalopathy, and 12 controls. Tissue-Doppler imaging and T-wave alternans were performed in the first 6 hours after birth in patients from both groups and after hypothermia-rewarming treatment on the fifth day. The basal T-wave alternans values were higher in patients in lead aVF ($p < 0.001$) which also correlated with existing acidemia ($r = 0.517$; $p = 0.012$). Basal T-wave alternans and post-treatment values of patients were compared in leads V1 ($p < 0.001$) and aVF ($p < 0.001$); a significant decrease was found on the fifth day. Moreover, right ventricle diastolic diameter and estimated systolic pulmonary artery pressure of patients in the first 6 hours were higher ($p = 0.03$, $p < 0.001$, respectively). Although, the ejection fraction of patients did not decrease, basal values of left and right ventricular systolic and diastolic functions were lower initially and increased significantly after treatment. Authors concluded that the global cardiac functions and myocardial performance of newborns with hypoxic-ischemia might be improved with therapeutic hypothermia which can be determined by using T-wave alternans and tissue-Doppler measurements. However, further studies are needed to assess whether these measurements are prognostic in determining the myocardial dysfunction and arrhythmias.

In a 2019 pilot study, Puljevic et al. investigated whether: a) MTWA can be new non-invasive tool for detection of reversible ischemia in patients with suspected coronary artery disease (CAD) without structural heart disease, b) MTWA can detect ischemia earlier and with greater test accuracy compared with exercise ECG ST-segment testing, and c) threshold value of MTWA and heart rate at which the alternans is estimated can be different compared to standard values. (10) A total of 101 patients with suspected stable coronary disease, but without structural heart disease, were included. Echocardiography, exercise ECG test, MTWA with classical and modified threshold alternans values, and coronary angiography were performed. About 33.3% patients had a false-positive result on exercise ECG test. The sensitivity of exercise ECG ST-segment test in the detection of CAD was 97.8%, and the specificity was 42.5% (DOR 33.89). In a group of angiographically positive patients, standard MTWA accurately identified 60% of patients, while 40% had a false-negative result. About 91.8% patients with negative angiography result were accurately identified with 8.2% false positives. The sensitivity of MTWA was 59.61% and specificity 91.83%. Best ratio of sensitivity and specificity (86.53% and 95.91%, DOR 151.06) had modified criteria for positive MTWA (MTWA >1.5 μV at heart rate 115–125/min). These small pilot study findings support that MTWA may be a new non-invasive tool for the detection of reversible ischemia in patients with suspected CAD without structural heart disease, and that MTWA can detect ischemia earlier and with greater accuracy compared with exercise ECG testing.

Xue et al. (2019) explored the characteristics of MTWA and its prognostic value when combined with an electrophysiologic study (EPS) in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). (11) All patients underwent non-invasive MTWA examination with modified moving average (MMA) analysis and an EPS. A positive event was defined as the first occurrence of sudden cardiac death, documented sustained ventricular tachycardia (VT),

ventricular fibrillation, or the administration of appropriate implantable cardioverter defibrillator therapy including shock or anti-tachycardia pacing. Thirty-five patients with ARVC (age 38.6 ± 11.0 years; 28 males) with preserved left ventricular (LV) function were recruited. The maximal TWA value (MaxValt) was 17.0 (11.0–27.0) μV. Sustained VT was induced in 22 patients by the EPS. During a median follow-up of 99.9 ± 7.7 months, 15 patients had positive clinical events. When inducible VT was combined with the MaxValt, the area under the curve improved from 0.739 to 0.797. The receiver operating characteristic curve showed that a MaxValt of 23.5 μV was the optimal cutoff value to identify positive events. The multivariate Cox regression model for survival showed that MTWA (MaxValt, hazard ratio [HR], 1.06; 95% confidence interval [CI], 1.01–1.11; *P* = 0.01) and inducible VT (HR, 5.98; 95% CI, 1.33–26.8; *P* = 0.01) independently predicted positive events in patients with ARVC. Authors concluded that MTWA assessment with MMA analysis complemented by an EPS might provide improved prognostic ability in patients with ARVC with preserved LV function during long-term follow-up. Despite a follow-up period as long as 8 years, the study was limited by a small sample size affiliated with a single center. ICD implantation was limited in the recruited patients. Furthermore, in this study, an update factor of 1/32 was used when analyzing TWA, which was less sensitive than the recommended update factor of 1/8. As a result, the TWA values obtained were substantially lower than expected, and the capacity to predict VT might also be reduced.

UpToDate

In a 2022 UpToDate review, it was noted that MTWA is primarily used as a tool for the risk stratification for sudden cardiac death, with much of the focus on patients with prior MI, reduced LV ejection fraction, and/or symptomatic heart failure. (12) The greatest utility of MTWA lies in its high negative predictive value and therefore in identifying those individuals at low-risk.

Practice Guidelines and Position Statements-MTWA

American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society (HRS)

The 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death state that “data on the use of microvolt T-wave alternans and the signal averaged ECG are inconclusive, as such these tests are not routinely used in clinical practice.” (13)

Signal-Averaged Electrocardiography (SAECG)

Literature Review

Use of signal-averaged ECG in risk stratification for ventricular arrhythmias

SAECG has been thoroughly studied as a risk stratification tool for potentially fatal arrhythmias in patients with a previous MI. As reviewed by the Agency for Health Care Policy and Research (AHCPR) in 1998, SAECG is associated with a low positive predictive value, ranging from 8–44%, depending on the population studied. (14) In contrast, the negative predictive value (i.e., the ability to identify those patients who will not experience ventricular arrhythmias) ranges from 88–97%, suggesting that the negative predictive value may be used to identify patients who

would not benefit from antiarrhythmic therapy. However, a key statistic underlying the negative predictive value is the underlying incidence rate of the outcome. Although sudden cardiac death is the most common cause of death in the 1-year period after infarction, it is relatively uncommon (2.5–11.3%) and declining, as a result of increasing use of thrombolytic therapy, aspirin, and beta-blockers. (15) Thus, given the relative low incidence rate of ventricular arrhythmias, the high negative predictive value is not surprising.

Grimm and colleagues reported on the results of the Marburg Cardiomyopathy study, a prospective observational study designed to determine the clinical value of potential noninvasive arrhythmia risk predictors among 343 patients with idiopathic dilated cardiomyopathy and followed up for 52 +/- 21 months for major arrhythmic events. (16) Reduced LVEF and lack of beta blocker use were important risk factors, but results of SAECG and T-wave alternans were not. Results of SAECG were found to only be a weak predictor of sudden cardiac death in a consecutive series of 700 patients with a history of acute myocardial infarction (AMI). (17) In another study of 1,800 consecutive survivors of AMI who underwent reperfusion therapy, late potentials identified by SAECG were not significantly associated with the endpoints of cardiac death or serious arrhythmias. (18)

In a 2018 article, Gatzoulis et al. noted that in the setting of healed MI, monomorphic VT is invariably caused by reentrant mechanisms, originating from myocardial sites located at the infarct border. (19) Accordingly, late potentials are recorded in nearly 90% of post-MI patients with a history of sustained monomorphic VT, as opposed to only ~20% in its absence. Moreover, SAECG is associated with high negative predictive value (>95%), with normal recordings strongly suggesting absence of a substrate for monomorphic VT; such inferences are supported by series of post-MI patients, reporting low incidence of arrhythmic events in patients with normal SAECG. Considering the high negative predictive value, SAECG may play an important role as a screening test in post-MI patients.

Use of signal-averaged ECG to select patients for anti-arrhythmic treatment
The ultimate validation of any diagnostic test is to determine how it is used in the management of patients and whether the management decisions result in improved health outcomes. The following discussion focuses on the clinical use of SAECG as a selection criterion for antiarrhythmic therapies in clinical trials.

A large number of randomized clinical trials (RCTs) have evaluated the effectiveness of either antiarrhythmic drugs or ICD implantation in post-MI patients. These trials have generally used a variety of risk stratification criteria to positively select patients for intervention. By selecting patients with a sufficiently high risk of arrhythmia, the benefits of treating arrhythmia will hopefully outweigh any adverse effects of the treatment. For the purposes of this discussion, the most relevant studies are those that look at patients who have not experienced a prior episode of near fatal ventricular arrhythmia or aborted sudden death. Patients with a prior history of a potentially fatal arrhythmia are already at sufficiently high risk and are considered candidates for either antiarrhythmic therapy or ICD.

The Coronary Artery Bypass Graft (CABG) Patch trial used SAECG as a positive patient selection criterion. (20) The CABG-Patch trial recruited patients scheduled for CABG who had an ejection fraction of less than 36% and abnormalities on SAECG. The use of SAECG was based on a pilot study that showed that an abnormal finding on SAECG was associated with a mortality rate that was double that seen in those with a normal SAECG in the 2 years after CABG. (21) Patients were randomly assigned to a defibrillator group or a control group, and all received CABG. After an average follow-up of 32 months, there was no evidence of improved survival among those in the defibrillator group. However, it cannot be determined whether the failure of this trial was due to the selection criteria or the treatments being compared.

Other trials investigating the use of ICD in post-MI patients have not provided clarity regarding the issue of risk stratification. The MADIT-II trial selected patients solely based on LVEF and showed a survival benefit among those randomly assigned to ICD. (22) No additional data have directly linked risk stratification information provided by SAECG to improved patient outcomes, improved efficiency, or reduced costs.

Use of signal-averaged ECG for other indications

Data are inadequate to evaluate the impact on patient management of other applications of SAECG including, but not limited to, its use in patients with cardiomyopathy; assessment of success after surgery for arrhythmia; detection of acute rejection of heart transplants; assessment of efficacy of antiarrhythmic drug therapy; assessment of success of pharmacological, mechanical, or surgical interventions to restore coronary artery blood flow; or risk stratification of patients with Brugada syndrome. Regarding the use of SAECG to identify patients with syncope who may have inducible VT, even though an ACC consensus document from 1996 concluded that SAECG had an established role, data from the report reported only modest sensitivity (73%) and poor positive predictive values. (23) Thus, if used to determine who should have electrophysiologic studies, the test will fail to detect many patients who have positive electrophysiologic studies.

In 2011, studies were also published on the utility of signal-averaged ECG for arrhythmogenic right ventricular cardiomyopathy, cardiac sarcoidosis, and epilepsy. (22-24) Kamath et al. (24) tested the utility of signal-averaged ECG in diagnosing arrhythmogenic right ventricular cardiomyopathy. These authors reported a sensitivity ranging from 47-69%, using different criteria for a positive test, and a specificity of 95%. Schuller et al. (26) reported a sensitivity of 52% and specificity of 82% for detecting cardiac involvement in patients with sarcoidosis. Rejdak et al. (25) studied 45 consecutive patients with epilepsy and compared results of signal-averaged ECG with 19 healthy controls. An abnormal signal-averaged ECG was found in 48% (22/45) of patients with epilepsy compared with 5% (1/19) of control patients.

In 2016, Dinov et al. looked at the correlation between SAECG and endocardial scar characteristics in patients with ischemic VT. (27) Fifty patients (42 male; aged 67±10 years, EF 34±12%) with ischemic VTs were prospectively enrolled. SAECG was performed before and after catheter ablation (CA). Patients with at least 2 abnormal criteria (filtered QRS ≥114 ms; root mean square 40 <20 μV, and low-amplitude potentials 40 >38 ms) were defined as having

positive SAECG. There was a linear correlation between endocardial scar area (<1.5 mV) and filtered QRS (r=0.414; P=0.003). CA resulted in normalization of the SAECG in 6 patients. In patients with filtered QRS ≤120 ms, 13 (40.6%) patients had normal SAECG after CA compared with 7 (21.9%) before ablation (P=0.034). Patients with normal or normalized SAECG after CA had better VT-free survival compared with those whose SAECG remained abnormal. Abnormal SAECG after CA was a predictor for VT recurrence: hazard ratio=3.64; P=0.039 for the overall population, and hazard ratio=5.80; P=0.022 for patients having QRS ≤120 ms. Authors concluded that there is a significant correlation between the surface SAECG and endocardial scar size in patients with ischemic VTs. A successful CA can result in normalization of SAECG that is associated with more favorable long-term outcomes. SAECG can be useful to assess the procedural success of VT ablation. However, study was limited by the small number and the relatively short follow-up of patients.

In a retrospective analysis, Nagamoto et al. (2017) evaluated the characteristics of the atrial arrhythmogenic substrate using the SAECG in patients with Brugada syndrome. (28) SAECGs were performed during normal sinus rhythm in 23 normal volunteers (control group), 21 patients with paroxysmal atrial fibrillation (PAF; PAF group), and 21 with Brugada syndrome (Brugada group). The filtered P wave duration (fPd) in the control, Brugada, and PAF groups was 113.9±12.9ms, 125.3±15.0ms, and 137.1±16.3ms, respectively. The fPd in the PAF group was significantly longer compared to that in the control and Brugada groups ($p<0.05$). The fPd in the Brugada group was significantly longer than that in the control group ($p<0.05$) and significantly shorter than that in the PAF group ($p<0.05$). The authors concluded that patients with Brugada syndrome had abnormal P waves on the SAECG. The abnormal P waves on the SAECG in Brugada syndrome patients may have intermediate characteristics between control and PAF patients. Prospective analysis is still needed to evaluate the development of AF in Brugada patients with an abnormal fPD.

Liao et al. (2017) looked at of SAECG in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) undergoing radiofrequency catheter ablation (RFCA) of ventricular arrhythmias. (29) Between 2010 and 2014, a total of 81 ARVD/C patients underwent endocardial and/or epicardial RFCA for drug-refractory VAs. Seventy patients (mean age 46.2±14.1years, 37 males) achieving acute procedure success (negative inducibility) were enrolled. Baseline characteristics, non-invasive examinations and SAECG (before and 3months after RFCA) were collected retrospectively. After successful RFCA, the electrical parameters of SAECG changed in 39 patients (55.7%), including 28 patients (40%) with electrical regression (group 1), and 11 patients (15.7%) with electrical progression (group 3). Thirty-one patients (44.3%) showed no significant SAECG change (group 2). During a mean follow-up of 17.8±10.7 months, 23 patients (32.9%) had VA recurrences, including 4 in group 1, 12 in group 2, and 7 in group 3. In comparisons with groups 2 and 3, group 1 patients had a significantly better VA recurrence-free survival (P=0.02). In multivariable Cox regression analysis, electrical regression was found to be associated with fewer VA recurrences (P=0.02, OR: 0.28, 95% CI: 0.10-0.83). The authors concluded that electrical regression of SAECG after RFCA in ARVD/C was found to be associated with fewer VA recurrences. Prospective, well-designed studies with larger sample sizes are needed to confirm these findings.

Chung et al. (2020) aimed to validate the role of SAECG in identifying arrhythmogenic substrates requiring an epicardial approach in ARVC. (30) Ninety-one patients with a definite diagnosis of ARVC who underwent successful ablation for drug-refractory ventricular arrhythmia were enrolled and classified into 2 groups: group 1 who underwent successful ablation at the endocardium only and group 2 who underwent successful ablation requiring an additional epicardial approach. Male predominance, worse right ventricular (RV) function, higher incidence of syncope, and depolarization abnormality were observed in group 2. Moreover, the number of abnormal SAECG criteria was higher in group 2 than in group 1. After a multivariate analysis, the independent predictors of the requirement of epicardial ablation included the number of abnormal SAECG criteria (odds ratio 2.8, 95% confidence interval 1.4–5.4; *P* = .003) and presence of syncope (odds ratio 11.7; 95% confidence interval 2.7–50.4; *P* = .001). In addition, ≥2 abnormal SAECG criteria were associated with larger RV endocardial unipolar low-voltage zone (*P* < .001), larger RV endocardial/epicardial bipolar low-voltage zone/scar (*P* < .05), and longer RV endocardial/epicardial total activation time (*P* < .001 and *P* = .004, respectively). Authors concluded that the number of abnormal SAECG criteria was correlated with the extent of diseased epicardial substrates and could be a potential surrogate marker for predicting the requirement of epicardial ablation in patients with ARVC. However, the study had a number of limitations and further prospective study will be warranted to validate the role of SAECG to predict the requirement of the epicardial approach in patients mivwith ARVC.

<u>UpToDate</u>

In a 2024 UpToDate review, it was stated that SAECG is rarely helpful and not routinely performed for diagnostic purposes in patients with documented sustained monomorphic ventricular tachycardia (SMVT). (31) It was further states that “Although the SAECG has a prognostic role for predicting the risk of SMVT in patients with ischemic heart disease, it has a limited role in the evaluation of patients who have already experienced SMVT and is rarely used in current cardiology practice.”

In an additional 2024 UpToDate review on ARVC, SAECG was identified as a “minor diagnostic criterion” and “not routinely employed”, a reflection of the fact that it has low sensitivity and specificity for the diagnosis of ARVC. (32) Few centers continue to utilize this diagnostic test for this reason.

<u>Practice Guidelines and Position Statements-SAECG</u>

American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society (HRS)

A 2017 clinical practice guideline from the American College of Cardiology/American Heart Association Task Force Clinical Practice Guidelines and the Heart Rhythm Society, developed in collaboration with the Heart Failure Society of America indicates that in patients with suspected arrhythmogenic right ventricular cardiomyopathy, a signal averaged ECG can be useful for diagnosis and risk stratification. (Strength of Recommendation: IIa [Moderate]; Level of Evidence: B-NR [nonrandomized]) (13)

Summary

Microvolt T-wave alternans (MTWA) is one available method to risk stratify patients who may be at risk for sudden cardiac death and has been proposed to assist in selecting patients for implantable cardioverter-defibrillators (ICD) treatment. Although results from prospective multicenter studies are insufficient to infer clinical utility, there is some evidence that MTWA may be useful in stratifying risk.

Signal-averaged electrocardiography (SAECG) has some ability to risk-stratify patients at risk for ventricular arrhythmias. However, this predictive ability is modest, and this technique has not been used to stratify patients into clinically relevant categories of risk. Some randomized controlled trials have used signal-averaged ECG for selection of patients at high risk of ventricular arrhythmias, but these studies have not demonstrated outcome benefits for the treatments under study. SAECG has also been tested as a diagnostic test for a variety of cardiac-related disorders, but the evidence is insufficient to demonstrate clinical utility for any of the conditions tested.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	93025, 93278
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position on microvolt T-wave alternans (MTWA). Within patient groups that may be considered candidates for implantable cardioverter defibrillator (ICD) therapy, a negative MTWA test may be useful in identifying low-risk patients who are unlikely to benefit from, and who may experience worse outcomes from, ICD placement. (33)

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <http://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
06/15/2025	Reviewed. No changes.
06/15/2024	Document updated with literature review. Coverage unchanged. Reference 13 added; others revised.
06/01/2023	Reviewed. No changes.
01/15/2023	Document updated with literature review. Coverage unchanged. Added references 12 and 30-32.
12/01/2021	Reviewed. No changes.
12/15/2020	Document updated with literature review. Coverage unchanged. Added references 4, 8-11, 18, 27-28; others removed.
11/15/2019	Reviewed. No changes.
11/01/2018	Document updated with literature review. Added the following statement to Coverage: “MTWA testing is considered experimental, investigational, and/or unproven for all other indications.” References modified, with the following new references added: 5-12, 17, 22-26.
10/15/2017	Reviewed. No changes.

10/01/2016	Document updated with literature review. Coverage unchanged.
08/01/2015	Reviewed. No changes.
11/15/2014	Document updated with literature review. Coverage unchanged. CPT/HCPCS code(s) updated
10/15/2013	Literature reviewed. No changes.
02/15/2009	Revised/updated entire document, this policy is no longer scheduled for routine literature review and update.
11/01/2006	Revised/updated entire document
08/15/2003	Revised/updated entire document
03/01/2002	Revised/updated entire document
04/01/1999	Revised/updated entire document
09/01/1998	Revised/updated entire document