News and Views from the Literature

Heart Failure

Microvolt T-Wave Alternans Testing to Target Patients for ICD Implantation and Prevent Sudden Cardiac Death

Reviewed by Norman E. Lepor, MD, FACC, FAHA

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Microvolt T-Wave Alternans and the Risk of Death or Sustained Ventricular Arrhythmias in Patients with Left Ventricular Dysfunction

Bloomfield D, Bigger J, Steinman R, et al.

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The use of automatic implantable cardiac defibrillators (AICDs) for the primary prevention of sudden cardiac death (SCD) in patients with either ischemic or nonischemic cardiomyopathy has been supported by data from several pivotal clinical trials including the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II and the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT).[1,2] This has led to recommendations from the American College of Cardiology/American Heart Association for the use of AICDs for primary prevention of SCD in patients with significant systolic dysfunction (left ventricular ejection fraction [LVEF] ≤ 30%) with either ischemic or nonischemic cardiomyopathy.[3]

Based on current implant volume, the use of AICDs constitutes an annual expenditure of $6 billion with expectations for significant growth, as only up to 15% of eligible patients have received them. Faced with this cost burden, The Center for Medicare and Medicaid Services will probably recommend the use of diagnostic testing using microvolt T-wave alternans (MTWA) to determine, with a higher level of specificity, who among currently AICD-eligible patients would be most likely to benefit from these lifesaving devices.

MTWA is a beat-to-beat fluctuation in the amplitude of the T-wave at a microvolt level. When detected, this phenomenon indicates the presence of a type of cellular metabolic activity that frequently leads to tachyarrhythmias. The proprietary Analytic Spectral Method algorithm measures alternans to as small as a millionth of a volt and processes the data to determine each patient's risk profile. Fourteen Sensors (7 micro-v alternans sensors and 7 standard electrodes) are placed in the Frank-lead configuration (Figure 1). These electrodes are connected to the digital ECG amplifier that leads back to the microvolt T-wave alternans-enabled system. The examination takes place with exercise (bicycle or treadmill) or pharmacologic stimulation. The presence of ectopy during the exam will reduce the ability to detect T-wave alternans accurately.

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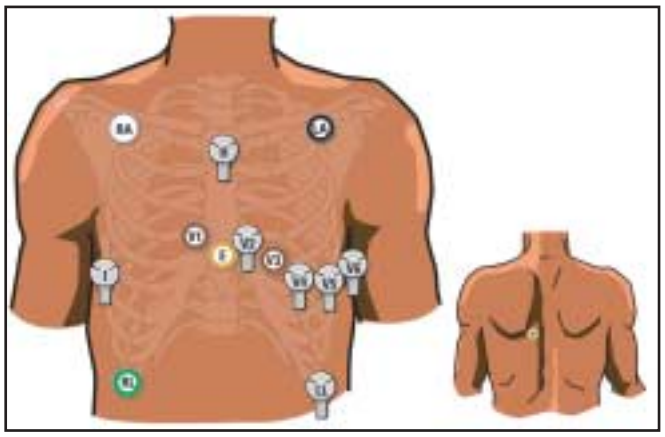

Figure 1. *Microvolt T-wave alternans are detected by utilizing 14 sensors (7 micro-v alternans sensors and 7 standard electrodes), placed in the Frank-lead configuration. These electrodes are connected to the digital ECG amplifier that leads back to the microvolt T-wave alternans-enabled system. The examination takes place with exercise (bicycle or treadmill) or pharmacologic stimulation.*

The study by Bloomfield and colleagues was performed at 11 clinical centers in the United States and evaluated 547 patients with LVEF measured at 40% or less. Patients were excluded if they had a history of sustained ventricular arrhythmias; atrial fibrillation; ventricularly paced, unstable, coronary artery disease; New York Heart Association (NYHA) Class IV heart failure; or if they were unable to exercise on a treadmill or bicycle. Patients underwent MTWA measurement using the CH2000 or HearTwave® systems (both Cambridge Heart, Inc., Bedford, MA). Baseline characteristics of the patients studied included: mean age of 56 years, 71% male, 28% with QRS duration greater than 120 msec, and an average LVEF of 25%. Fifty percent of patients had ischemic heart disease with two-thirds designated in NYHA Functional Classes II or III. Eighty percent were treated with β-blockers and angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs). The primary endpoint of this trial included all-cause mortality and nonfatal sustained ventricular arrhythmias, including AICD shocks with intracardiac electrograms documenting rapid ventricular tachycardia or ventricular fibrillation within the past 2 years. An MTWA test was performed at the beginning of the trial and was abnormal in 66% of patients. The 2-year actuarial event rate was 15% in the patients with an abnormal MTWA exam and 2.5% in those with an abnormal exam, yielding a hazard ratio of 6.5 (CI, 2.4-18; $P < .001$). See Figure 2.

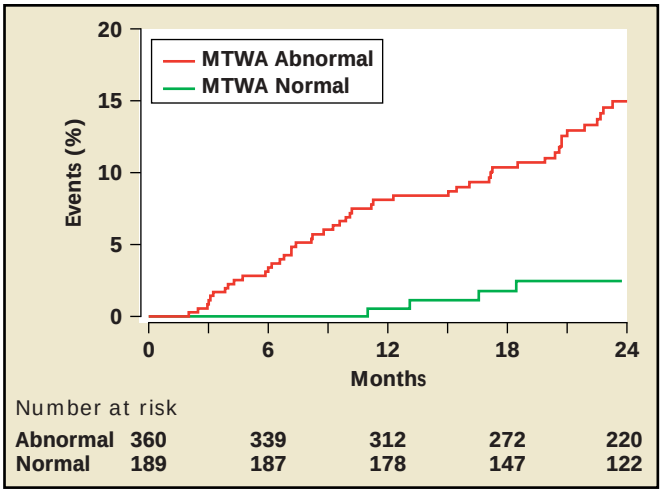

Figure 2. *Kaplan-Meier mortality curves for patients with normal versus abnormal microvolt T-wave alternans (MTWA) test results. Reproduced with permission from Bloomfield et al.* J Am Coll Cardiol. *2005;0:j.jacc.2005.11.026v1-11647.*

Besides an abnormal MTWA, the only other risk predictors relating to the primary outcome on univariate analysis were a lack of β-blocker administration, incidence of recent heart failure hospitalization, and gender.

The authors conclude that MTWA can define both a high- and low-risk group of left-ventricular-dysfunction heart failure patients for the occurrence of sudden cardiac death. Data from this examination only allow us to define risk within 20 months of the MTWA administration, as this was the mean follow-up period in the trial. We cannot use this examination to assess risk further out in time from the initial test. The possibility that serial testing in low-risk patients will be necessary, in order to assess possible conversion to a positive MTWA and define a change in risk status, will need to be evaluated in further clinical trials. Another interesting issue is that of whether patients who convert to a negative MTWA at some point can be re-evaluated and classified in terms of SCD risk from a high- to a characteristically low-risk group.

Rather than reducing the number of AICD implants, which are currently utilized in only 15% of eligible patients, the use of the MTWA should lead to greater use of this lifesaving technology, as 66% of patients studied were positive and placed into the higher-risk group. Wide use of this examination in AICD-eligible patients should motivate both the cardiologist and the patient to have a device implant if the test is abnormal. However, the 34% of patients who test negative for MTWA and are placed into a low-risk group may avoid an AICD placement altogether, or be postponed until there is a conversion to a positive MTWA. These patients can be maximally treated with the contemporary heart failure cocktail of β-blockers, ACE inhibitors/ARBs, aldosterone antagonists, and hydralazine/nitrates. AICD placement can be delayed

until the MTWA converts to positive or avoided altogether in those who remain normal. A safe interval between tests in patients who are normal has not been quantified but, based on the results of this trial, may be every 2 years. Because this study excluded patients with atrial fibrillation and inability to exercise on a treadmill/bicycle or NYHA Class IV heart failure, the MTWA test cannot currently be used to risk stratify for SCD in these patients. ■

References

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Patients at Risk

Air Pollution and Heart Disease

Reviewed by Karol E. Watson, MD, PhD

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Ambient Air Pollution Is Associated With Increased Risk of Hospital Cardiac Readmissions of Myocardial Infarction Survivors in Five European Cities

von Klot S, Peters A, Aalto P, et al.; Health Effects of Particles on Susceptible Subpopulations (HEAPSS) Study Group.

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Air pollution has been found to be associated with increased morbidity and mortality in the general population, primarily related to respiratory effects, but also related to cardiovascular disease. The Health Effects of Particles on Susceptible Subpopulations (HEAPSS) Study has followed cohorts of first myocardial infarction survivors in 5 European cities: Augsburg (Germany), Barcelona (Spain), Helsinki (Finland), Rome (Italy), and Stockholm (Sweden), assessing the air pollution-related risks in this population. Using the HEAPSS cohort and correlating hospital admissions with several markers of urban air pollution (particle number concentration [PNC], mass of particles < 10 µm [PM_{10}], carbon monoxide [CO], nitrogen dioxide [NO_2], and ozone), the investigators assessed whether ambient air pollution was associated with increased cardiac hospital readmissions in survivors of myocardial infarction.

Methods and Results

Myocardial infarction survivors (N = 22,006) were recruited in the 5 cities between 1992 and 2000. First subsequent cardiac rehospitalizations within the study area were recorded from the 29th day after the index event until the center-specific end of the follow-up period. Readmissions were recorded for those with primary diagnoses of acute myocardial infarction, angina pectoris, dysrhythmia, and heart failure. Air pollution data from fixed monitors were collected for each city and daily means were calculated for each pollutant in each city.

During the follow-up, 2321 hospital readmissions for myocardial infarction, 3541 for angina pectoris, and 6655 for cardiac events were observed among the 22,006 HEAPSS cohort members. Same-day levels of air pollutants were significantly associated with cardiac readmissions. This study found a 2.1% increase in cardiac hospital admissions for every 10 µg/m^3 increase in the mass of particles < 10 µm (PM_{10}). This effect ratio is larger than that seen in prior studies.

Conclusions and Interpretation

In this multicenter cohort study of myocardial infarction survivors, an increased risk of cardiac readmissions during days with elevated concentrations of several markers of urban air pollution (PNC, PM_{10}, CO, NO_2, and ozone) was observed.

Whereas other studies had observed an association between cardiovascular morbidity and mortality and air pollution in the general population, this study was specifically designed to examine this association in a cohort of potentially vulnerable subjects (ie, those with prior myocardial infarction). This study showed positive and generally larger effects than studies conducted in the general population. Therefore, myocardial infarction survivors might, in fact, be more susceptible to air pollution-related cardiovascular events than members of the general population. ■