

## **Microvolt T-wave Alternans and Electrophysiological Testing Predict Different Arrhythmia Outcomes: Lessons from the Alternans Before Cardioverter Defibrillator (ABCD) Trial**

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**Background:** Although microvolt T-wave Alternans (MTWA) and electrophysiological study (EPS) are both markers for sudden cardiac death (SCD), the ABCD trial, found the combination to be more predictive than each alone. Therefore, we hypothesized that the two tests measure elements of the arrhythmogenic substrate, which lead to different arrhythmic outcomes.

**Methods:** The ABCD Trial included 566 patients with ischemic cardiomyopathy, left ventricular ejection fraction (LVEF)  $\leq 0.40$ , and documented non-sustained ventricular tachycardia. All patients underwent both MTWA test and EPS at enrollment. Implantable cardioverter defibrillators (ICD) were implanted in 87% of patients. The primary end-point was first appropriate ICD therapy or SCD. MTWA and EPS Core Laboratories blinded to outcomes adjudicated the tests, and an Events Committee blinded to the results of the tests adjudicated all events. Using Kaplan-Meier event rates and the log rank test, we analyzed the performance of MTWA and EPS in predicting distinct arrhythmic outcomes: 1. monomorphic ventricular tachycardia (MVT) vs. 2. the combination of polymorphic ventricular tachycardia (PVT) or ventricular fibrillation (VF) or SCD.

**Results:** MTWA was normal in 29% and abnormal in 71%, and EPS was negative in 61% and positive in 39% of patients. There were 42 MVT events and 24 PVT/VF/SCD events, (8.8% and 5.6% 2-year event rate, respectively). At 1-year, MTWA predicted PVT/VF/SCD (event rate: 2.7% vs. 0% for MTWA abnormal vs. normal;  $p=0.04$ ), but not MVT. In contrast, EPS predicted MVT (event rate 9.7% vs. 2.2% for EPS + vs. EPS -;  $p<0.01$ ), but not PVT/VF/SCD. At 2 years MTWA was not a significant predictor of either arrhythmia outcome, but a positive EPS remained predictive of MVT (14.7% vs. 4.7%;  $p<0.01$ ). Finally, LVEF (dichotomized by LVEF  $\leq 0.30$ ) was not predictive of either arrhythmia outcome.

**Conclusions:** MTWA and EPS differ in the arrhythmic outcome they predict, and the time frame of prediction, suggesting that they identify different arrhythmogenic substrates. These data further suggest that multiple risk markers used in combination may better define and predict the complex electro-anatomical substrates which underlie the risk of SCD.