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Presentation Title: Predictive Accuracy of Microvolt T-Wave Alternans Testing in Primary Prevention Patients With and Without ICDs

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Introduction: Microvolt T-wave alternans (MTWA) testing has proven in many studies to be a highly accurate predictor of ventricular tachyarrhythmic events (VTEs) in patients with risk factors for sudden cardiac death but without a prior history of sustained VTEs (primary prevention patients). In some recent studies MTWA has not performed as well. In the present analysis we examine the hypothesis that MTWA is an accurate predictor of VTEs in patients without implanted ICDs, but not of appropriate ICD therapy (AICD-Rx) in patients with prophylactically implanted ICDs.

Methods: We identified prospective clinical trials evaluating MTWA measured using the spectral analytic method in primary prevention populations and analyzed studies in which (1) few patients had implanted ICDs and $\leq 15\%$ of reported endpoint VTEs were AICD-Rx or (2) a majority of reported endpoint VTEs were AICD-Rx.

Results: In the low AICD-Rx group comprising 3,682 patients the hazard ratio associated with a non-negative vs negative MTWA test was 13.6 [8.5-30.4] (brackets denote 95% confidence interval, $p < 0.0001$), and the annual event rate (AER) among MTWA negative patients was 0.3% [0.1%-0.5%]. In contrast, in the high AICD-Rx group comprising 2,234 patients the hazard ratio was only 1.6 [1.2-2.1] ($p < 0.001$), and the AER among MTWA negative patients was elevated to 5.4% [4.1%-6.7%]. In support of these findings we analyzed published data from the MADIT II and SCD-HeFT trials and determined that in those trials only 32% of patients who received AICD-Rx averted SCD.

Conclusions: MTWA testing provides an accurate means of predicting SCD in primary prevention patients without implanted ICDs; in particular, the event rate is very low among patients with a negative MTWA test. In prospective trials of ICD therapy the number of AICD-Rx's greatly exceed the number of SCDs that would have occurred in the absence of ICD implantation. In trials involving patients with implanted ICDs these excess AICD-Rx's appear to distribute randomly between MTWA negative and non-negative patients obscuring the predictive accuracy of MTWA for SCD. AICD-Rx is an unreliable surrogate for SCD in clinical trials.

"These results demonstrate that MTWA is a consistently accurate predictor of sudden cardiac death and cardiac arrest in patients who do not already have implanted ICDs. These are the patients for whom MTWA testing is intended."

- Dr. Stefan Hohnloser, J. W. Goethe University, Frankfurt, Germany