

Letter to the Editor

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*Title*

**Microvolt T-wave alternans testing provides a reliable means of guiding anti-arrhythmic therapy**

*Abbreviated Title*

**Microvolt T-wave alternans testing**

**Authors**

Stefan H. Hohnloser, M.D.

Department of Cardiology

Division of Electrophysiology

J.W. Goethe University

Frankfurt, Germany

Richard J. Cohen, M.D., Ph.D.

Harvard-MIT Division of Health Sciences and Technology

Massachusetts Institute of Technology

Cambridge, Massachusetts

Email: [rjcohen@mit.edu](mailto:rjcohen@mit.edu)

Telephone: 617-253-7430

Fax: 617-253-3019

Gupta et al<sup>1</sup> present a meta-analysis and conclude that microvolt T-wave alternans testing (MTWA) does not modify risk of sudden cardiac death (SCD) sufficiently for clinical use. Their analysis involves a number of methodological limitations. The authors included in their primary analysis numerous surrogates for sudden cardiac death (SCD) such as ICD therapy, cardiac mortality and total mortality. It has been demonstrated<sup>2,3</sup> that use of such surrogates introduces spurious endpoints several fold greater in number than the number of actual SCD events. The authors also did not adjust for duration of follow-up - combining equally studies with follow-ups ranging from 13 to 52 months. The authors also used historical event rates from studies<sup>4,5</sup> not included in their meta-analysis to calculate expected event rates rather than using the event rates from the studies in the meta-analysis itself.

The authors base their analysis on the likelihood ratio (LR) with the justification that this statistic is population independent. LR, like sensitivity and specificity, is theoretically population independent only to the extent that the population is composed of a binary mixture of individuals. In practice, all statistical measures may be population dependent and one cannot assume that results from one population may be reliably extrapolated to another. Expected event rates bifurcated by test result combined with the expected benefit/risk of the intervention are among the most important parameters for clinical decision making.

The most relevant sub-analysis presented by the authors is the one that excluded the surrogate endpoints mentioned above. The authors reported that for this sub-analysis  $LR+ = 1.79$  and  $LR- = 0.34$ . Applying these LRs to the SCD annual event rate that the authors derive from SCD-HeFT<sup>4</sup> (more recent than MADIT-II<sup>5</sup> data) yields expected annual SCD rates of 5.2% and 1.0%.

These results match well with the actually measured rates of 4.2% and 0.9% in 1004 patients with LVEF  $\leq$  0.35 from a recent pooled analysis<sup>6</sup>.

No study has ever demonstrated a benefit for ICD therapy in a patient population with an SCD rate anywhere close to as low a level as 0.9% per year. ICD implantation itself is associated with an in-hospital mortality of approximately 1% and a high complication rate subsequent to implantation<sup>7</sup>. Conversely, patients with a non-negative MTWA test have SCD event rates which are greater than the event rates in the studies for which ICD therapy was demonstrated to provide a mortality benefit. Moreover, ICD therapy has been directly demonstrated to provide a mortality benefit only in patients with a non-negative MTWA result but not in patients with a negative result<sup>8</sup>.

Consistent with other analyses<sup>3,6,8</sup> the results of Gupta et al<sup>1</sup> - when surrogate endpoints are excluded - indicate that, in fact, MTWA testing is an accurate and reliable means of guiding anti-arrhythmic therapy.

## **References**

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