Microvolt T-wave alternans testing to risk stratify patients being considered for ICD therapy for primary prevention of sudden death
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CRD summary
This review found there to be insufficient evidence on which to base conclusions about the use of microvolt T-wave alternans testing to risk stratify patients being considered for implantable cardioverter defibrillator therapy for the primary prevention of sudden death. Given the limitations of the review, the results should be viewed with caution. However, the authors’ conclusions seem suitably cautious.

Authors’ objectives
To evaluate the efficacy of microvolt T-wave alternans (MTWA) to risk stratify patients who might be considered for implantable cardioverter defibrillator (ICD) therapy.

Searching
MEDLINE was searched to May 2005; the search terms were reported. The Cochrane Library was also searched, and the manufacturer of MTWA contacted. Only articles published in English in peer-reviewed journals that were full length, or provided sufficient information about study design, methods and results, were included.

Study selection
Study designs of evaluations included in the review
Prospective studies were eligible for inclusion. Case reports were excluded. The designs of the included studies were not reported.

Specific interventions included in the review
Studies of MTWA, performed according to stress protocol with a commercially available device, were eligible for inclusion. No further details were provided.

Reference standard test against which the new test was compared
There were no inclusion criteria relating to the reference standards. The authors discussed the reference standards available; these included invasive electrophysiology, signal averaged electrocardiogram, heart rate variability, baroreflex sensitivity and Holter monitoring. However, the reference standards used in the individual included studies were not reported.

Participants included in the review
Studies of patients who might be considered for ICD therapy were eligible for inclusion. The populations recruited into the included studies comprised patients with coronary artery disease, idiopathic dilated cardiomyopathy, acute myocardial infarction, electrophysiology, congested cardiac failure and Brugada syndrome, and Multicenter Automatic Defibrillator Implantation Trial II-like patients.

Outcomes assessed in the review
The studies had to report event rates stratified by MTWA results, the sensitivity and/or specificity of MTWA, or a Kaplan-Meier analysis. The main outcomes of interest were morbidity, mortality and quality of life. The outcomes reported in the included studies were ventricular tachycardiac events (VTE), death (cardiac, sudden cardiac, non-sudden cardiac, all-cause) and cardiac arrest.

How were decisions on the relevance of primary studies made?
The authors did not state how the studies were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The authors did not state that validity was assessed.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Event rates and diagnostic measures (sensitivity, specificity, positive and negative predictive values and likelihood ratios) were extracted from each study.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative, grouped by eligibility for ICD placement and the predictive value of MTWA. Pooled analyses conducted by other authors were presented as supplementary material.

How were differences between studies investigated?
Details of the studies and their results were tabulated, and differences between the studies were discussed in the text. Results for patients with a left ventricular ejection fraction (LVEF) of more than 30% were discussed separately.

Results of the review
Eighteen studies (n=2,931) were included in the review.

In patients eligible for ICD placement who are undecided whether to go ahead, MTWA results may be used to support decision-making: it may be used for either its positive or negative predictive value (PPV and NPV, respectively).

MTWA predicting VTE: the sensitivity ranged from 75 to 100% and the specificity from 38 to 88% (9 studies). Therefore, for eligible patients seeking an ICD, MTWA may assist in the identification of patients at low risk of subsequent VTE who would be unlikely to benefit from an ICD.

Patients with negative MTWA results have a 3.8 to 16% risk of death during follow-up (4 studies); event-free survival ranged from 80 to 100% at 1 and 2 years (4 studies).

In patients with an LVEF of more than 30%, the NPV of MTWA is generally high. Two studies showed no events in participants with negative MTWA and LVEF greater than 30%; one study of questionable validity reported an NPV of 73%.

In patients eligible for ICD placement who are undecided whether to go ahead, abnormal MTWA results may support the use of ICD implantation; the PPV of MTWA for VTE was 7 to 73%, with likelihood ratios of 1.4 to 6.3 (9 studies). For all-cause mortality, the PPV was 40% and the likelihood ratio 1.4 (95% confidence interval: 1.1, 1.8; 2 studies). Event rates amongst MTWA-positive patients ranged from 7 to 31% for VTE; 0 to 40% subsequently died.

For patients not eligible for an ICD, the PPV and likelihood ratio of MTWA could assist in the identification of patients with clinically suspected VTE who may benefit from ICD placement.

Authors’ conclusions
There is insufficient evidence relating to health outcomes to determine the effects of MTWA testing for risk stratifying patients being considered for ICD therapy for the primary prevention of sudden death.

CRD commentary
The review question was clear though the inclusion criteria for study design were broad. The authors conducted a limited search of only English language articles and, whilst some attempts were made to locate unpublished data, the review may be at risk of both publication and language bias. The authors did not state whether methods were used to reduce error and bias during the study selection and data extraction processes. Study quality did not appear to have been
assessed and study designs were not identified, so the validity of the findings was unclear. However, the narrative synthesis seemed appropriate given the differences between the studies. Overall, given the aforementioned limitations of the review, the results should be viewed with caution. However, the authors' conclusions seem suitably cautious.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

**Bibliographic details**
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