



Enhancing Specificity Without Sacrificing Sensitivity: Potential Benefits of Using Microvolt T-Wave Alternans Testing to Risk Stratify the MADIT-II Population

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Abstract. The MADIT-II study (Moss et al., *N Engl J Med* 2002;346:877–883) demonstrated that implantation of a cardioverter/defibrillator (ICD) reduced mortality from 19.8% to 14.2% during 20 months of follow-up in patients with prior myocardial infarction and left ventricular ejection fraction ≤ 0.30 . Concerns have been raised both about the cost and potential morbidity of implanting ICDs in a large group of patients when only a small fraction of the patients would be expected to benefit from the treatment. This concern has given rise to the hope that an effective means of risk stratifying the MADIT-II population might be developed so that ICD therapy can be directed to only those patients who are at significant risk and thus likely to benefit from treatment for purposes of primary prevention of arrhythmic death. Electrophysiology study (EPS) is probably not suitable for this purpose because of its established relatively high false negative rate and because it is itself an invasive procedure. QRS width has been proposed for this purpose but prospective data demonstrating its effectiveness in stratifying the MADIT-II population for risk of arrhythmic death are absent. Initial data suggest that microvolt T-wave alternans (MTWA) testing does appear to be a suitable candidate for risk stratifying the MADIT-II population. These data indicate that approximately 30% of the MADIT-II population test negative for MTWA and that these patients are at extremely low risk for sudden cardiac death and cardiac arrest. Furthermore, MTWA is an inexpensive non-invasive test which can be repeated over time to monitor whether a patient who initially tests negative develops arrhythmic risk with the progression of the underlying disease. As studies of MTWA testing in the MADIT-II population come to publication, a database will likely be formed which will establish MTWA as an effective means of stratifying the MADIT-II population. ICD therapy may not be indicated in patients who test MTWA negative, and conversely the remaining patients may enjoy a greater mortality benefit than that observed in the MADIT-II trial. Furthermore, widespread MTWA testing might have the further benefit in those patients who do not test negative of serving as a call to action to referring physicians to direct those patients to ICD therapy, thereby greatly increasing the number of appropriate patients who actually receive potentially life saving therapy.

Key Words. alternans, sudden death, cardiac arrest, defibrillator, T-wave, ICD

The MADIT-II trial [1] demonstrated that in patients with prior myocardial infarction and left ventricular ejection fraction ≤ 0.30 that implantation of an implantable cardioverter/defibrillator (ICD) reduced mortality from 19.8% to 14.2% over an average of 20 months of follow-up. The authors of the study estimated that there are approximately 400,000 new MADIT-II type patients each year in the United States, and that proceeding with ICD therapy in all MADIT-II patients would represent a significant cost to the health care system. In addition, placing ICDs in all MADIT-II patients would involve an invasive and expensive therapy for a large cohort of patients of which only a small fraction would be expected to benefit from the therapy. This is of concern because implantation of an ICD has morbidity associated with it. In this regard it is interesting to note that the authors of the MADIT-II study observed a higher incidence of hospitalization for heart failure in patients with ICDs than in the control group, although a causative relationship between ICD implantation and increased incidence of new or worsened heart failure was not established. While it is possible that the mortality benefit of ICD therapy might be greater than 5.6% over a longer duration of follow-up, that has not been proven at this point, and the benefit of ICD therapy would likely still be limited to a small fraction of the patients treated.

As a result of the medical concern of subjecting such a large group of patients to invasive therapy, and as a result of the concern related to the cost to the health care system of treating the entire MADIT-II population with ICDs, there has been increasing interest in the potential of subdividing the

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