Microvolt T-wave alternans testing has a role in arrhythmia risk stratification.

Richard L. Verrier, PhD, Thomas Klingenheben, MD, Marek Malik, PhD, MD, Nabil El-Sherif, MD, Derek V. Exner, MD, MPH, Stefan H. Hohnloser, MD, Takanori Ikeda, MD, Juan Pablo Martínez, PhD, Sanjiv M. Narayan, MD, PhD, Tuomo Nieminen, MD, PhD, David S. Rosenbaum, MD

Boston, Massachusetts; Bonn and Frankfurt, Germany; London, England; Brooklyn, New York; Calgary, Alberta, Canada; Tokyo, Japan; Zaragoza, Spain; San Diego, California; Helsinki, Finland; and Cleveland, Ohio

Word count: 496 words, 7 references

Correspondence:
Dr. Marek Malik
St. George's University of London
Cranmer Terrace
London SW17 0RE, United Kingdom.
E-mail: marek.malik@btinternet.com.

In one interesting aspect, the letter by Dr Jackson et al[1] pertains to risk stratification in general. They suggest that evidence-based cardiac risk assessment should be an automatic process devoid of individual clinical judgment. We disagree and maintain that any risk assessment requires careful interpretation by experienced physicians. Unfortunately, the Glasgow group misrepresented our guideline statement[2] not only in this respect.

The presence of abnormal T-wave alternans (TWA) has demonstrated clinical utility in stratifying risk for malignant arrhythmias and sudden cardiac death. This derives from prospective, peer-reviewed studies involving >12,000 patients. These data clearly show that patients with increased TWA levels have 2- to 23-fold independently higher risk of serious outcomes as compared with those with lower TWA levels. Elevated TWA provides risk information independent of left ventricular ejection fraction (LVEF), standard clinical variables (e.g., age and sex) and important cardiovascular risk markers (e.g., smoking, diabetes, hypertension, and medication usage). Our assertion, "it is reasonable to consider TWA evaluation whenever there is suspicion of vulnerability to lethal cardiac arrhythmias," concurs with prior statements by the American Heart Association, the American College of Cardiology,[3,4] and the National Institutes of Health.[5]

As with any risk stratification method, including LVEF, not all studies are consistent with the overall trend. Specifically, in the Microvolt T-wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients (MASTER) trial and TWA substudy of Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), TWA did not predict the development of appropriate implantable cardioverter defibrillator (ICD) therapy, sudden cardiac death, and/or ventricular

tachycardia/fibrillation. As discussed in our document, there are plausible explanations for this departure from the bulk of the literature. Specifically, a recent systematic review and meta-analysis determined that withdrawal of beta-adrenergic blockade before TWA assessment diminishes its predictive strength by nearly 4-fold.[6] This observation also applies to the reduced predictivity in other prospective studies. Furthermore, it carries the important implication that TWA is sensitive to chronic therapy,[7] supporting our assertion that TWA assessment should be performed while patients are on their usual, chronic medications.

Regarding the potential application of TWA to guide therapy, we stated, "there is as yet no definitive evidence from interventional trials that it can guide therapy." However, this conclusion does not connote an absence of evidence or the impossibility of using TWA to support other risk markers, especially in borderline cases. The Alternans Before Cardioverter Defibrillator (ABCD) trial demonstrated that TWA testing appears to be comparable to electrophysiologic study in guiding ICD implantation and that the two methods may be complementary. Numerous studies outlined in our document demonstrate that TWA provides additive predictive value to LVEF and other risk stratifiers. These facts are reflected in our recommendation that TWA should not be used as a sole parameter either to rule in or to rule out the prescription of ICD therapy.

Thus, even without dedicated trials on therapy guidance, a sizeable number of prospective studies support TWA's utility in risk stratification for life-threatening arrhythmias and its potential value in clinical judgment.

1. Jackson CE, Myles RC, Cobbe SM, et al. Microvolt T-wave alternans testing has no role at present in guiding therapy for patients at high risk of ventricular arrhythmias [letter]. J Am Coll Cardiol, in press.
2. Verrier RL, Klingenheben T, Malik M, et al. Microvolt T-wave alternans: Physiologic basis, methods of measurement, and clinical utility. Consensus statement by the International Society for Holter and Noninvasive Electrocardiology in collaboration with Japanese Circulation Society, Computers in Cardiology Working Group of European Society of Cardiology, and European Cardiac Arrhythmia Society. J Am Coll Cardiol 2011; 58:1309–24.
3. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a Report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol 2006; 48:e247–346.
4. Goldberger JJ, Cain ME, Hohnloser SH, et al. American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society Scientific statement on noninvasive risk stratification techniques for identifying patients at risk for sudden cardiac death. A scientific statement from the American Heart Association Council on Clinical Cardiology Committee on Electrocardiography and Arrhythmias and Council on Epidemiology and Prevention. J Am Coll Cardiol 2008; 52:1179–99.

5. Fishman GI, Chugh SS, DiMarco JP, et al. Sudden cardiac death prediction and prevention: report from a National Heart, Lung, and Blood Institute and Heart Rhythm Society workshop. Circulation 2010;122:2335– 48.
6. Chan PS, Gold MR, Nallamothu BK. Do beta-blockers impact microvolt T-wave alternans testing in patients at risk for ventricular arrhythmias? A meta-analysis. J Cardiovasc Electrophysiol 2010; 21: 1009–14.
7. Verrier RL, Nieminen T. T-wave alternans as a therapeutic marker for antiarrhythmic agents. J Cardiovasc Pharmacol 2010; 55(6):544-554.