Journal of the American College of Cardiology
© 2000 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 36, No. 7, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(00)01017-2

A Comparison of T-Wave Alternans, Signal Averaged Electrocardiography and Programmed Ventricular Stimulation for Arrhythmia Risk Stratification

Michael R. Gold, MD, PHD, FACC,* Daniel M. Bloomfield, MD, FACC,†
Kelley P. Anderson, MD, FACC,‡ Nabil E. El-Sherif, MD, FACC,§ David J. Wilber, MD, FACC,‖
William J. Groh, MD, FACC,†† N. A. Mark Estes, III, MD, FACC,#
Elizabeth S. Kaufman, MD, FACC,†† Mark L. Greenberg, MD, FACC,**
David S. Rosenbaum, MD, FACC**

Baltimore, Maryland; New York, and Brooklyn, New York; Pittsburgh, Pennsylvania; Chicago, Illinois; Indianapolis, Indiana; Boston, Massachusetts; Cleveland, Ohio; Lebanon, New Hampshire

OBJECTIVES The goal of this study was to compare T-wave alternans (TWA), signal-averaged electrocardiography (SAECG) and programmed ventricular stimulation (EPS) for arrhythmia risk stratification in patients undergoing electrophysiology study.

BACKGROUND Accurate identification of patients at increased risk for sustained ventricular arrhythmias is critical to prevent sudden cardiac death. T-wave alternans is a heart rate dependent measure of repolarization that correlates with arrhythmia vulnerability in animal and human studies. Signal-averaged electrocardiography and EPS are more established tests used for risk stratification.

METHODS This was a prospective, multicenter trial of 313 patients in sinus rhythm who were undergoing electrophysiologic study. T-wave alternans, assessed with bicycle ergometry, and SAECG were measured before EPS. The primary end point was sudden cardiac death, sustained ventricular tachycardia, ventricular fibrillation or appropriate implantable defibrillator (ICD) therapy, and the secondary end point was any of these arrhythmias or all-cause mortality.

RESULTS Kaplan-Meier survival analysis of the primary end point showed that TWA predicted events with a relative risk of 10.9, EPS had a relative risk of 7.1 and SAECG had a relative risk of 4.5. The relative risks for the secondary end point were 13.9, 4.7 and 3.3, respectively ($p < 0.05$). Multivariate analysis of 11 clinical parameters identified only TWA and EPS as independent predictors of events. In the prespecified subgroup with known or suspected ventricular arrhythmias, TWA predicted primary end points with a relative risk of 6.1 and secondary end points with a relative risk of 8.0.

CONCLUSIONS T-wave alternans is a strong independent predictor of spontaneous ventricular arrhythmias or death. It performed as well as programmed stimulation and better than SAECG in risk stratifying patients for life-threatening arrhythmias. (J Am Coll Cardiol 2000;36:2247–53)

Accurate identification of patients at increased risk for sustained ventricular arrhythmias is critical for the development of effective strategies to prevent sudden cardiac death. Traditionally, left ventricular ejection fraction and measures of ambient arrhythmia were used to identify high-risk cohorts and to evaluate the utility of the prophylactic administration of antiarrhythmic drugs (1). Unfortunately, this strategy has not proven beneficial in reducing mortality (2–5). Recently, programmed ventricular stimulation during electrophysiology (EPS) testing (6,7), but not signal averaged electrocardiography (SAECG) (8), identified a cohort with left ventricular dysfunction who had improved survival with implantable cardioverter-defibrillator (ICD) placement. However, programmed stimulation is invasive and costly. Accordingly, improved noninvasive markers of arrhythmia vulnerability are needed. In this regard, T-wave alternans (TWA) is a promising new technique (9).

See page 2254

T-wave alternans is a heart rate-dependent measure of repolarization (10). Previously, TWA induced with atrial pacing was shown to predict ventricular arrhythmias in patients undergoing EPS (11). Subsequently, techniques were developed to allow assessment of alternans noninvasively with exercise. There is a high concordance between exercise-induced and pacing-induced TWA (12). Moreover, TWA measured noninvasively predicts the induction of ventricular tachyarrhythmias at EPS (13) as well as appropriate discharges in patients with ICDs (14). However, the predictive value of TWA measured noninvasively in patients undergoing arrhythmia evaluation is unknown.

From the *Department of Medicine, Division of Cardiology, University of Maryland Medical System, Baltimore, Maryland; †Columbia Presbyterian Medical Center, New York, New York; ‡University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, §Veterans Affairs Medical Center, Brooklyn, New York; ‖University of Chicago Hospitals, Chicago, Illinois; ¶Indiana University, Indianapolis, Indiana; #New England Medical Center, Boston, Massachusetts; **MetroHealth Campus, Case Western Reserve University, Cleveland, Ohio, and ††Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire. Supported by a grant from Cambridge Heart, Inc., Bedford, Massachusetts.

Manuscript received February 22, 2000; revised manuscript received August 2, 2000, accepted August 11, 2000.