T-Wave Alternans Testing for Ventricular Arrhythmias

Sanjiv M. Narayan

T-wave alterans (TWA) measures alternate-beat fluctuations in the ECG T-wave, and has been used to predict the risk for life-threatening ventricular arrhythmias in various clinical populations. This work reviews the traditional literature linking repolarization alternans in cellualr and tissue-level studies, with clinical studies that TWA can successfully add to existing clinical risk factors in predicting ventricular arrhythmias. We conclude by providing an evidence-based framework integrating TWA with other risk factors to stratify risk for sudden cardiac arrest.

Sudden cardiac arrest (SCA) from ventricular arrhythmias is the largest cause of death in industrialized countries and claims more than 300,000 lives in the United States per year.[1] Unfortunately, identifying individuals at risk for this fate remains challenging, as does the task of optimally identifying potential recipients of the implantable cardioverter-defibrillator (ICD). Although reduced systolic function[2] and heart failure[3] identify risk, they lack specificity.

T-wave alternans (TWA) is a promising electrocardiogram (ECG) index of arrhythmic susceptibility that has been shown to provide a high negative predictive value for ventricular arrhythmias[4] and thus identify individuals who may not benefit from ICD implantation.[5] T-wave alternans measures beat-to-beat fluctuations in the timing or shape of the ECG T wave and was first observed nearly a century ago.[6,7] Visible TWA has since been linked with arrhythmias in the long QT syndrome,[8] electrolyte abnormalities,[9] and ischemia[10] and, over time, has been detected at increasingly subtle levels (Fig 1). Contemporary TWA testing uses ECG signal processing to detect oscillations on the order of microvolts that are invisible to the unaided eye yet related mechanistically to visible TWA.[4]

From the University of California and VA Medical Center, La Jolla, CA.

Address reprint requests to Sanjiv M. Narayan, MB, MD, FACC, FRCP, Associate Professor, University of California San Diego, Whitaker Institute for Biomedical Engineering Cardiology, 111A, 3350 La Jolla Village Dr, San Diego, CA 92161. E-mail: snarayan@ucsd.edu

0033-0620/$ - see front matter

doi:10.1016/j.pcad.2007.11.001

Pathophysiology of TWA

A wealth of bench-to-bedside studies show that alternans of intracardiac repolarization (action potential duration [APD]) may directly initiate ventricular arrhythmias in animals[15,16] and may be linked with human microvolt-level TWA.[17,18] These mechanistic studies provide unique scientific validation to TWA as a risk stratifier, although some details on the link between TWA and human arrhythmias remain unclear.[17,18]

T-Wave Alternans and Spatial Repolarization Dispersion

The left panel of Fig 2 shows spatial repolarization dispersion between regions 1 and 2. Action potential duration is longer in region 1 than 2 and so, at fast heart rates, region 1 may still be repolarizing and fail to depolarize every-other-beat.[19] Regions of long APD may also be sites of block where reentry initiates.[20] Ischemia or extrasystoles may exaggerate spatial dispersion in animals[21] and amplify human TWA.[22] Under critical conditions, such factors may reverse the phase of cellular alternans so that juxtaposed regions alternate out-of-phase. The interface (nodal lines) between such *discordant* regions can be sites of unidirectional block that lead to reentry.[15,16]

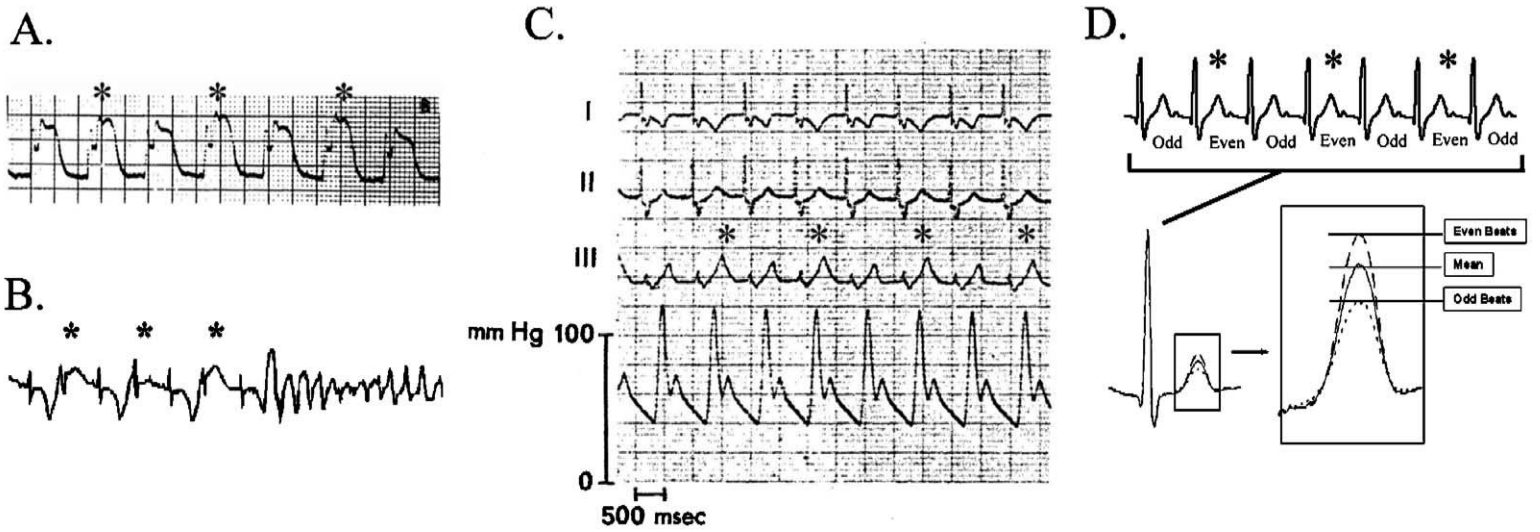

Fig 1. Historical evolution: detecting T-wave alternans of increasing subtlety. A, Extreme alternans of elevated ST/T segments in a patient with angina pectoris preceding VT [11]; B, Visible alternans of T-wave polarity, preceding VF [12]; C, Subtle but visible TWA after tachycardia termination, without arterial pressure alternans (bottom) [13]; D, Visually inapparent microvolt-level TWA, extracted by signal processing.[14] Asterisk indicates the more positive T wave of each alternating pair. Panels A to C reprinted with permission.