Clinical significance of microvolt T-wave alternans

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Several studies have recently proven that primary preventive therapy of sudden arrhythmogenic death is possible in selected patients with congestive heart failure, particularly in the setting of ischemic cardiomyopathy [1, 2]. However, a number needed to treat between 11 and 17 to save one life over three years in these studies indicates that a more accurate identification of high risk patients is desirable in order to avoid unnecessary implants of cardioverter/defibrillators (ICD). Since currently available risk stratification methods have limited predictive accuracy, development of new techniques is important in order to non-invasively assess arrhythmogenic risk in patients prone to sudden death. Microvolt level T-wave alternans (mTWA) has recently been proposed to assess abnormalities in ventricular repolarization favoring the occurrence of reentrant arrhythmias [3, 4]. In 1994, a first clinical study by Rosenbaum and coworkers [5] convincingly demonstrated that mTWA is closely related to arrhythmia induction in the electrophysiology (EP) laboratory as well as to the occurrence of spontaneous ventricular tachyarrhythmias during follow-up [5]. More recently, a number of clinical studies has examined its clinical applicability [4–7]. The present review summarizes currently available clinical data on TWA with a particular focus on risk stratifying patients with congestive heart failure and myocardial infarction.

Key words arrhythmia risk stratification – T-wave alternans – left ventricular function
Definition, pathophysiological aspects, and methodology of TWA

T-wave alternans is defined as 2:1 beat-to-beat changes in the amplitude of the T-wave. Whereas visible “macroscopic” TWA has been associated with a high risk of ventricular tachyarrhythmias in patients with the congenital long QT syndrome [6] or other clinical disorders, this phenomenon is rarely observed in clinical practice. With the development of new computer processing techniques, the phenomenon of microvolt level TWA (mTWA) was first demonstrated in an experimental study by Adam, Smith and coworkers [3, 7]. Recent experimental and clinical studies have provided new insights into the genesis of this phenomenon [4, 8–10]. Briefly, with increasing heart rate, action potential duration shows discordant prolongation in different regions of the myocardium finally resulting in repolarization alternans with opposite phase between neighboring cells (so-called discordant alternans). This creates increased spatial dispersion of repolarization associated with unidirectional conduction block, reentry, and finally the occurrence of ventricular fibrillation [4]. On the cellular level, TWA is accompanied by inhomogeneities in the calcium transient indicating that Ca^{2+} ions play a key role in the genesis of TWA [11].

The methodology of mTWA assessment is described in detail elsewhere [12]. Briefly, during increasing heart rate (either exercise test or atrial pacing) sequential ECG cycles are aligned to their QRS complex and the amplitude of the T waves at a predefined point \( t \) are measured. Subsequently this beat-to-beat series of amplitude fluctuations are subjected to spectral analysis using fast Fourier transformation. TWA manifests itself as a pronounced peak which is visible in the spectrum at 0.5 cycles/beat. An alternans voltage exceeding 1.9 μV with the alternans ratio \( K \) (indicator of the significance of the measurement) being \( \geq 3 \) is defined significant (Fig. 1).

Clinical validation of microvolt TWA

In their first clinical study comprising 83 patients undergoing invasive EP study, Rosenbaum et al. demonstrated that mTWA assessed during atrial pacing was predictive both of the results of invasive EP testing as well as of arrhythmic events [5]. Survival analysis revealed that mTWA performed as well as EP testing in prediction of arrhythmic events during follow-up. The 20-month survival probability free of recurrent arrhythmia was significantly lower in mTWA positive patients (19 vs. 94%, \( p < 0.01 \) [5]). These observations were later substantiated in a multicenter study involving 313 patients (LVEF 44±18%, coronary disease in

Fig. 1 Alternans voltage in a patient with moderately reduced left ventricular function and a history of syncope following myocardial infarction. Note the increase of TWA voltage with increasing heart rate (HR)