Is there a role of MMA T wave alternans test for risk assessment in Brugada syndrome?

Brugada sendromu risk değerlendirmesinde MMA T dalga alternansının rolü var mı?

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Brugada syndrome (BS) is a genetic disease that is characterized by persistent or transient ST elevation in right precordial electrocardiogram (ECG) leads with or without right bundle branch block and increased risk of sudden cardiac death with a structurally normal heart (1). Previous studies have suggested that depolarization and repolarization abnormalities are involved in the occurrence of polymorphic ventricular tachycardia (VT) or ventricular fibrillation (VF) (2), but the precise pathophysiologic mechanisms are still unclear. Risk stratification in BS is still controversial. Implantable cardioverter-defibrillators (ICDs) are inserted to the patients experienced cardiac arrest, syncope and whose ECG showed type I pattern, inducible ventricular arrhythmia with programmed ventricular stimulation (3). A report by Raju et al. (4) demonstrated that the majority of individuals experiencing BS sudden death are asymptomatic before their terminal event and 68% of surviving patients has no ICD indication according to current guidelines. Furthermore, some patients showing Brugada type ECG may not have a tendency to arrhythmias (5). Additional methods are needed to identify patients who would benefit from ICD implantation.

Assessment of microvolt T wave alternans (TWA) is a promising method proposed for risk stratification for sudden cardiac death (SCD) (6). TWA is a beat-to-beat variation in T wave amplitude related to spatial and/or temporal variations of ventricular repolarization that several experimental studies have shown to be associated with increased vulnerability to ventricular arrhythmias (7). Microvolt TWA has been shown in patients with BS particularly following exposure to sodium channel blockers (8). Cellular mechanism of TWA in Brugada syndrome can be due to alternating loss of epicardial action potential dome and/or con-

cealed phase 2 reentry, which may create the substrate for the development VT/VF (9).

In clinical practice, two methods for assessing microvolt TWA are available, spectral and modified moving average (MMA) methods. Experience with the Spectral method is more extensive. The MMA method employs the noise-rejection principle of recursive averaging. The algorithm continuously streams odd and even beats into separate bins and creates median complexes for each bin. These complexes are then superimposed, and the maximum difference between the odd and even median complexes at any point within the JT segment is averaged for every 10 to 15 s and reported as the TWA value. The moving average allows control of the influence of new incoming beats on the median templates with an adjustable update factor (i.e., the fraction of morphology change that an incoming beat can contribute). The recommended rapid update factor of one-eighth provides greater sensitivity and capacity to detect transient but clinically important surges in TWA than one-sixteenth or one-thirty-second (10). Noise measurements are in part derived from mismatch of the even or odd median complexes outside the JT segment. The algorithm excludes extrasystoles, noisy beats, and the beats preceding them and filters effects of noise, movement, and respiration. The methods are analytically comparable, although they differ in noise processing. Hazard ratios for arrhythmia prediction by the Spectral and MMA methods are similar, whether in the same population or in studies overall (11). It has been reported that microvolt TWA, assessed by spectral method was not a predictor of arrhythmic events in Brugada syndrome (12). On the other hand after infusion of pilsicainide; a Na channel blocker occurrence of macroscopic TWA
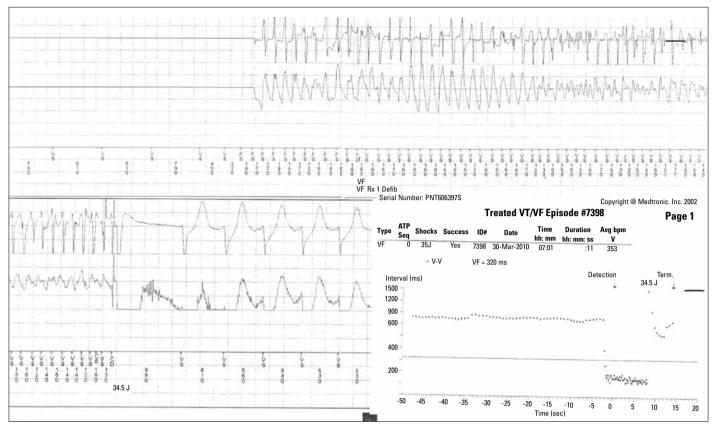
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Figure 1. EGM recording of a patient with appropriate ICD shock due to VF
EGM - electrogram, ICD - implantable cardioverter defibrillator, VF - ventricular fibrillation, VT - ventricular tachycardia

was associated with a high risk of clinical VF in patients with BS (13). However, microvolt TWA, assessed by MMA method in this patient group has not studied yet. We therefore investigated the prevalence of microvolt TWA and the association between spontaneous ventricular arrhythmia occurrences in high-risk BS patients.

For this study, we prospectively included 13 patients with BS (M/F: 12/1). All patients presented with either syncope (n=10) or aborted sudden cardiac death requiring defibrillation (n=3). Physical examination, echocardiography and coronary angiography were normal in all patients. Family history of sudden cardiac death was positive in 3 of BS patients. There was a spontaneous type I ECG in 7 patients. Type 1 ECG unmasked by ajmaline in 6 patients. Twelve of patients underwent an electrophysiological study: 6 of them had induced ventricular arrhythmias. An ICD was implanted to nine patients. Other four patients refused the implantation of an ICD, one patient was lost to long term follow up (Table 1). All patients underwent TWA testing at the time of diagnosis. We used 4th intercostal space for V1 and V2 electrodes. TWA was assessed with the MMA method, 16 using the software provided by the EST system manufacturer (GE CASE 8000, Millwaukee, WI, USA). Briefly, with this method a sequence of beats are separated into odd and even beats. Along the entire J-T segment, separated average morphologies of both the odd and even beats are calculated separately and continuously updated to every new incoming beat by a weighting factor of 1 of 8 in order to minimize the influence of noise on

the TWA measurement and, then, to get a higher reliability of this method. The TWA value is calculated as the maximal difference between the averages of odd and even beats along one of the J-T-segment sampled points in any lead. TWA is analyzed continuously during the entire stress test and the recovery phase up to heart rate of 125 bpm. Three values of TWA were considered; one derived from the analysis of all 12 leads (TWAtot), one derived from the analysis of the 6 precordial leads only (TWAprec), and one derived from the analysis of the V1-3 leads only (TWA_V1-3). This second measure was performed because T wave is often better identifiable in the precordial rather than in the peripheral leads. The third measurement was performed because V1-3 leads were affected in BS. Cut off value for TWA was 65 µV for all three measurements as done in previous studies (10). The data were counted valid only if the noise level was less than 10 µV. The mean TWAtot was 18.7 +/-6.8, TWAprec was 17.0+/-6.9, TWAV1-3 was 15.5+/-5.5, respectively. All of the measurements were considered as negative tests.

During follow up of mean 22+/-8 months, three of ICD patients had ventricular arrhythmia requiring ICD discharge (Fig. 1), two of patients had inappropriate shocks (one was due to sinus tachycardia, one was due to T wave over sensing). In these patients, TWA tests were negative. Our data agrees with another previously published study on TWA in BS (12).

This study extends that report in three ways: First, this study demonstrates that MMA TWA cannot be detected in Brugada patients at high risk for sudden death. Second, analysis of TWA in

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Table 1. Clinical characteristics of Brugada syndrome patients

Variables	n
Male sex	12/13
Median age	31 years
Syncope	10/13
Survived SCD	3/13
Family history of SCD	3/13
Defibrillator implantation	9/13
VT/VF inducibility on EPS	6/13
Spontaneous type I ECG	7/13
Positive Na^+ channel blocker challenge test	6/13

ECG - electrocardiogram, EPS - electrophysiologic study, SCD - sudden cardiac death, VF - ventricular fibrillation, VT - ventricular tachycardia

the predominant locations of ECG changes in Brugada syndrome, i.e., in the right ventricular precordial leads, does also not identify high-risk Brugada syndrome patients. Third, TWA was also negative in patients who had spontaneous ventricular arrhythmia during follow up. Despite microvolt TWA by MMA, is a promising test for identification of sudden death in various heart diseases, it is not an appropriate tool for risk stratification of BS.

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