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

To the Editor,

We read with interest the scientific letter by Drs. Yalin et al. (1) in The Anatolian Journal of Cardiology on the null outcome of their T-wave alternans (TWA) analysis by the Modified Moving Average method in patients with the Brugada syndrome. To date, TWA has been found in only two studies (2, 3) to predict lethal arrhythmias in Brugada syndrome patients, despite the fact that it is a prominent feature in their ambulatory ECG (AECG) recordings (4). Tada and colleagues (2) reported in a case series of 77 Brugada syndrome patients that overt TWA provoked by pilsicainide predicted spontaneous ventricular fibrillation with odds of 22.2 (95% CI: 3.3-149.9, p<0.001) after multivariate analysis. Most recently, Uchimura-Makita and coworkers (3) used MMA-based TWA in a case series of 42 Brugada syndrome patients and reported that the incidence of VF events was significantly higher among those with TWA ≥60μV than in those with lower TWA levels in lead V2 (p=0.0026).

Dr. Yalin et al. (1) indicated that TWA testing was performed at the time of diagnosis of Brugada syndrome but did not state whether the patients were undergoing an exercise stress test or were at rest. While no studies have been undertaken to examine the optimum recording conditions for TWA analysis, it is reasonable to expect that TWA testing should be performed in conjunction with a diagnostic stressor such as the sodium channel blocking agents ajmaline, flecainide, procainamide, pilsicainide (2, 5), which unmask the Brugada syndrome (6), or during spontaneous appearance of the diagnostic Brugada ECG during daily activity at more normal heart rates (7), as is captured on AECG recordings. Indeed, the presence of TWA is considered to support the diagnosis of Brugada syndrome in asymptomatic patients with ST-segment elevation in at least one right precordial lead (6). Nighttime may be a particularly suitable period for AECG recording for TWA analysis, as the majority of ventricular fibrillation episodes in Brugada syndrome patients occur during sleep (8). The finding that TWA level is greatly reduced when heart rate is increased to 80-110 beats/min (7), such as is reached during exercise, may be the key to the failure of TWA testing by the spectral method (9, 10). If TWA had been analyzed from AECGs recorded during daily activity or sleep, it is likely that many if not all of the Brugada syndrome patients enrolled in this study may have shown significant levels of TWA.

Determining the most appropriate setting for TWA testing in Brugada Syndrome patients will be an important contribution to stratification of their risk for lethal arrhythmias and ICD discharge.

We compliment Dr. Yalin and colleagues on the valuable contributions of their study.

With best regards,

Richard L. Verrier
Harvard Medical School, Beth Israel Deaconess Medical Center, Division of Cardiovascular Medicine, Harvard-Thorndike Electrophysiology Institute; Boston-*USA*

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Address for Correspondence: Dr. Richard L. Verrier, F.A.C.C., Associate Professor of Medicine, Harvard Medical School Beth Israel Deaconess Medical Center, 99 Brookline Avenue, RN-301B Boston MA 02215-*USA*
Phone: 617-667-0730
Fax: 617-975-5270
E-mail: rverrier@bidmc.harvard.edu
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Author`s Reply

Dear Editor;

We would like to thank Dr. Verrier for his comments and interest in our work published in Anadolu Kardiyol Derg 2013; 13: 702-4. (1). He raised some important points that we would like to discuss.

First; he asked whether the patients was at rest or was undergoing an exercise stress test to perform T wave alternans test. All patients underwent an exercise stress test to achieve higher heart rates. This condition may not be appropriate for Brugada patients. In Brugada

syndrome (BS), ventricular fibrillation (VF) occurs mainly during sleep, and Brugada ECG signs are intensified by parasympathomimetic drugs; therefore, vagal activity could be a precipitating factor of VF; Mizumaki et al. (2) stated that spontaneous augmentation of ST elevation in daily life occurred along with an increase in vagal activity. Performing T wave alternans (TWA) test under exercise stress test that favours sympathetic stimulation may supress microvolt T wave alternans level.

Performing the test under a sodium channel blocker, such as ajmaline to unmask type I Brugada ECG, may be considered. But in our study patients seven of them had pretest spontaneous type I ECG and the result of modified moving average (MMA) TWA were also negative in these patients. Ajmaline may induce sustained ventricular arrhythmias in BS patients. Conte et al. (3) performed ajmaline challenge test to 503 patients and 9 patients (1.8%) developed life threatening ventricular tachyarrhythmias. Two of their cases were resistant to first external defibrillation and one of them underwent venoarterial extracorporeal membrane oxygenation to restore sinus rhythm. The reason we did not infuse Na channel blocker to study patients is that, safety of ajmaline administration to BS patients while exercise stress test is unknown.

The prognostic value of these non-invasive ECG indices remains equivocal in BS patients. This may be explained in part by dynamic instability of the ECG features of BS; they are known to be concealed or unmasked by autonomic activity, food intake, body temperature and a variety of drugs. Such problems could be circumvented by extensive analysis of ambulatory ECGs, taking circadian periodicity into account (4). Yoshioka et al. (5) and Abe et al. (6) studied ambulatory ECGs of BS patients and showed the dynamic daily variations in late potantials and T wave amplitude variability. We agree with Dr. Verrier that the analyzing of TWA from AECGs from our high risk BS cohort could show significant levels of TWA.

In summary, MMA TWA test performing under exercise test for risk stratification in BS is not useful. TWA test should be studied in this cohort analyzing AECGs.

Kıvanç Yalın, Ebru Gölcük, Ahmet Kaya Bilge
Department of Cardiology, İstanbul Faculty of Medicine, İstanbul University; İstanbul-*Turkey*

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Address for Correspondence: Dr. Kıvanç Yalın,
İstanbul Üniversitesi İstanbul Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Çapa İstanbul-*Türkiye*
Phone: +90 212 414 20 00
E-mail: yalinkivanc@gmail.com
Available Online Date: 18.12.2013

YKL-40 levels in patients with coronary artery ectasia

To the Editor,

We have read the article "Increased YKL-40 levels in patients with isolated coronary artery ectasia (CAE): an observational study" written by Erdoğan et al. (1) in Anadolu Kardiyol Derg 2013; 13: 465-70. with great interest. They aimed to investigate YKL-40 and C-reactive protein (CRP) levels in patients with isolated CAE compared to patients with normal coronary arteries and coronary artery disease (CAD). They concluded that YKL-40 levels in patients with isolated CAE compared to patients with NCA were found significantly high and only YKL-40 level was established as the determinant of CAE.

Some conditions may increase quality of the present study. Firstly, the CAE classification is an important condition for study design. The CAE classification previously described by Markis et al. (2). YKL-40 level may be different in severity of CAE according to Markis classification. For this reason, if the authors had mentioned, the results of the study could be useful.

Although the etiopathogenesis of CAE is not very well defined, we considered that endothelial dysfunction contributes to the atherosclerotic process (3). In 85% of the cases, CAE is accompanied by atherosclerotic CAD. Multiple factors contribute to the pathogenesis of atherosclerosis, but inflammation and oxidative stress are likely to play a role. Because metabolic syndrome (4), abnormal thyroid function tests, renal or hepatic dysfunction, known malignancy (5), inflammatory diseases (6), and any medication (7) that related to inflammatory condition of patients, the measurement of YKL-40 levels can be potentially affected in all of above conditions. For these reasons, it would be better, if the authors had mentioned these factors.

Obstructive sleep apnoea syndrome (OSAS) and non-alcoholic fatty liver disease (NAFLD) are common in clinical practice. Cardiovascular complications are common in patients with OSAS have been linked to morbidity and mortality in these patients (8). Also, the presence and the degree of NAFLD are associated with higher inflammatory parameters. Additionally, common pathways involved in the pathogenesis of NAFLD includes subclinical inflammation, and atherosclerosis (9). In this point of view, because NAFLD and OSAS are associated with atherosclerosis and inflammation, future studies should mention these factors.