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ORIGINAL ARTICLE

Microvolt T-Wave Alternans in Patients with a Biventricular Implantable Defibrillator

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ABSTRACT

OBJECTIVE: Microvolt T-wave alternans (MTWA) was found to be associated with cardiac electrical instability. The aim of this study was to investigate the effects of biventricular pacing on MTWA in comparison with other pacing modalities.

METHODS: The study group consisted of 50 patients with dilated or ischemic cardiomyopathy with a cardiac resynchronization therapy device. MTWA was measured during several pacing modalities.

RESULTS: Overall, 181 MTWA studies were performed in 50 patients. Seventy-nine studies (44%) were negative, 81(45%) were positive and 21 (12%) were indeterminate. With right atrial (RA) pacing, 45% of the MTWA tests were negative. With right ventricular (RV) pacing, 30 % were negative, with left ventricular (LV) pacing 44 % were negative and with biventricular pacing 52% of the tests were negative (P=0.15). The results of TWA testing were concordant between RA pacing and biventricular pacing (K=0.46, P=0.007).

CONCLUSION: Microvolt T-wave alternans during biventricular pacing correlates with MTWA during atrial pacing and left ventricular pacing.

KEY WORDS: *T wave alternans; heart failure; cardiac pacing; cardiac resynchronization*

List of Abbreviations

AV = atrio-ventricular
CRT = cardiac resynchronization therapy
ICD = implantable cardioverter defibrillator
IVCD = intra-ventricular conduction
LBBB = left bundle branch block
LV = left ventricle
MTWA = microvolt T wave alternans
RA = right atrium
RBBB = right bundle branch block
RV = right ventricle

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INTRODUCTION

Microvolt T-wave alternans (MTWA) measures subtle beat-to-beat variations in the T wave during exercise or during rapid atrial pacing. Microvolt T-wave alternans was found to be associated with cardiac electrical instability in patients with ischemic and dilated cardiomyopathy.[1-7] These patients suffer from heart failure and benefit from cardiac resynchronization therapy (CRT). There have been conflicting reports on the electrical effects of biventricular pacing. Some reports showed a beneficial effect[8] and others showed no effect[9] or a detrimental effect with biventricular pacing.[10]

The purpose of this study was to systematically measure MTWA in 4 pacing modes (right atrial pacing, right ventricular pacing, left ventricular pacing and biventricular pacing). Our hypothesis was that a better synchronization of contraction between both ventricles may be electrically beneficial.

METHODS

PATIENT POPULATION

The study group consisted of 50 patients with dilated or ischemic cardiomyopathy referred to Assaf Harofeh Medical Center during the period of August 2003 to October 2009. All patients had a left ventricular ejection fraction of <35%. All patients underwent a biventricular defibrillator or pacemaker implantation for treatment of heart failure. Patients with atrial fibrillation and patients with atrioventricular (AV) block were also included. Patients on antiarrhythmic agents and beta blockers were also included and were tested on their chronic medications. Informed consent was obtained from all study subjects.

MEASUREMENT OF MICROVOLT T-WAVE ALTERNANS

All subjects were prospectively evaluated for MTWA using 4 different pacing modes via a pacemaker or an implantable cardioverter defibrillator (ICD). The patients were paced using the AAI mode, DDD mode with right ventricle (RV) only, DDD mode with left ventricle (LV) only and DDD mode with simultaneous RV and LV pacing. The AV delay was programmed at 180 ms. The patients were paced at 110 beats per minute (bpm) for 5 minutes at each pacing mode. After each test the pacing mode was programmed back to biventricular pacing at the original settings for 10 minutes. The HearTwave™ system from Cambridge heart was used (Cambridge Heart Inc., Bedford, MA, USA). The system uses the spectral method described by Smith et al.[2] After careful skin preparation, 7 standard electrodes were placed in the standard 12-lead position and 7 multi-segment special electrodes were arranged in a Frank orthogonal (XYZ) configuration.

The MTWA test was automatically interpreted within the HearTwave™ system and reviewed by a physician. The test was considered positive if the alternans voltage was ≥1.9 Volts and the alternans ratio was ≥3 for a period of >1 minute in vector magnitude (VM), X, Y, Z, or 2 adjacent precordial leads with an onset heart rate ≤110 beats/min during pacing. The test was considered negative if alternans was absent during a sustained interval of pacing at a heart rate of 110 beats/min. If the result did not meet the positive or negative criteria, it was considered indeterminate. The MTWA results were categorized as negative and non-negative results (which included the positive and indeterminate results) for the purpose of data analysis.

The patients were seen in the arrhythmia clinic every 6 months and had their pacemaker or ICD interrogated and the device telemetry checked for possible arrhythmias.

STATISTICAL ANALYSIS

We compared the parameters of patients with a positive MTWA and the patients with a negative MTWA. We used the chi-square test for the categorical variables and the independent sample t–test for the continuous variables. Results are presented as mean ± standard deviation. Concordance of MTWA test results during RA pacing with pacing from other sites was evaluated using the Cohen Kappa test and the Bonferroni post-hoc analysis. Statistical analysis was performed using an SPSS version 13 software. A P value of <0.05 was considered statistically significant.

RESULTS

PATIENT CHARACTERISTICS

The clinical characteristics of the 50 patients studied are presented in Table 1.

MICROVOLT T-WAVE ALTERNANS TESTING

Each patient underwent 4 consecutive MTWA studies

TABLE 1. Patient characteristics

	Positive MTWA with biventricular pacing n=23	Negative MTWA with biventricular pacing n=27	P value
Age (years)	65.4 ± 10.4	66.4.9 ± 11.81	ns
Male, n	20	21	ns
Diagnosis, n			
CAD	17	18	ns
CMP	6	9	
Beta blockers, n	20	27	0.053
Amiodarone therapy, n	7	9	ns
Sotalol therapy, n	3	2	ns
LV electrode site, n			
Lateral wall	7	10	
Posterolateral wall	8	12	ns
Epicardial	2	2	
Unknown	6	3	
ICD Therapy			
NO	14	20	ns
Yes	9	7	
Time from implant to MTWA test (ms)	7.46 ± 13.1	11.30 ± 16.75	ns
Follow up from MTWA test (ms)	9.78 ± 7.56	13.9 ± 6.70	ns

CAD = coronary artery disease, CMP = cardiomyopathy, ICD = implantable cardioverter defibrillator; MWTA = microvolt T-wave alternans; ns = non-significant using 4 different pacing modes. Overall, 181 MTWA studies were performed. Seventy-nine (44%) were negative, 81(45%) were positive and 21 (12%) were indeterminate. Nine patients had Wenckebach during atrial pacing, 5 patients had atrial fibrillation and could not be atrially paced, 3 patients were pacemaker dependent and could not be paced in the AAI mode and 2 patients did not tolerate rapid LV only pacing because of chest discomfort.

With right atrial (RA) pacing, 45% of the MTWA tests were negative. With RV pacing, 30 % were negative, with LV pacing 44 % were negative and with biventricular pacing 52% of the tests were negative (P=0.15). Patients on beta blockers were more likely to have a negative MTWA in the biventricular pacing mode (P=0.053) (Table 1).

Concordance rates for MTWA were used to compare RA, RV and LV pacing to biventricular pacing (Table 2). The results of MTWA testing were concordant between RA pacing and biventricular pacing (K=0.46, P=0.007), and they were concordant between LV and biventricular pacing (K=0.50, P=0.0001). The results of MTWA were not concordant between RV pacing and biventricular pacing (K=0.184, P=0.01), between LV and RV pacing (K=0.126, P=0.067), between RA and RV pacing (K=0.309, P=0.062), and between LV and RA pacing (K=0.135, P=0.135).

The data were analyzed also according to the baseline QRS morphology prior to device implantation. Thirty patients had a left bundle branch block (LBBB) and 20 patients had a non-LBBB which included right bundle branch block (RBBB), non-specific intra-ventricular conduction (IVCD) and a narrow QRS complex. Table 3 summarizes the details of this analysis. Right ventricular pacing seemed to be more detrimental in patients who did not have a LBBB morphology on their baseline ECG (P=0.035).

Two patients died during the follow-up period of 11.7± 7 months. One patient had a negative MTWA in all 4 pacing modes and died from pump failure and the second patient had an indeterminate result in all 4 pacing modes and died from a ruptured aortic aneurysm.

TABLE 3. Results of MTWA during the different pacing modes in patients with LBBB compared to patients without LBBB in their baseline ECG.

	N	LBBB no	LBBB yes	P value
BIV - non negative	50	10	13	ns
BIV - Negative		10	17	
RA - non negative	33	7	11	ns
RA - Negative		4	11	
RV - non negative	50	17	17	0.035
RV - Negative		3	13	
LV - non negative	48	11	16	ns
LV - Negative		8	13	

BIV = biventricular; ECG = electrocardiogram; LBBB = left bundle branch block; LV = left ventricle; MTWA = microvolt T-wave alternans; ns = non-significant; RA = right atrium; RV = right ventricle

DISCUSSION

Microvolt T-wave alternans (MTWA) is a relatively new noninvasive method for identifying patients at increased risk of sudden cardiac death from ventricular arrhythmias.[2] It measures subtle beat to beat fluctuations in the T wave amplitude. Microvolt T-wave alternans is heart rate dependent and can be measured during an exercise stress test, during pharmacologic stress or during cardiac pacing.[11,12] Clinical studies have shown a good correlation between MTWA and the results of electrophysiological studies in patients with ischemic heart disease.[2] More recent studies have shown mixed results about the capacity of MTWA to predict sudden death, sustained ventricular arrhythmias or appropriate ICD discharges.[17-21]

The present study provides the largest series to date, of patients who underwent a MTWA testing during 4 different pacing modes. This study indicates that MTWA during bi-

TABLE 2. Concordance of MTWA results with the different pacing modes.

	RA N=33		RV N=50		LV N=48	
	Non negative	Negative	Non negative	Negative	Non negative	Negative
BIV - non negative	12	3	18	5	19	4
BIV - Negative	6	12	16	11	8	17
Concordance	72.7%		58%		79.2%	
Kappa	K=0.459 P=0.007		K=0.184 P=0.151		K=0.503 P=0.000	

BIV = biventricular; LV = left ventricle; MTWA = microvolt T-wave alternans; RA= right atrium; RV= right ventricle.

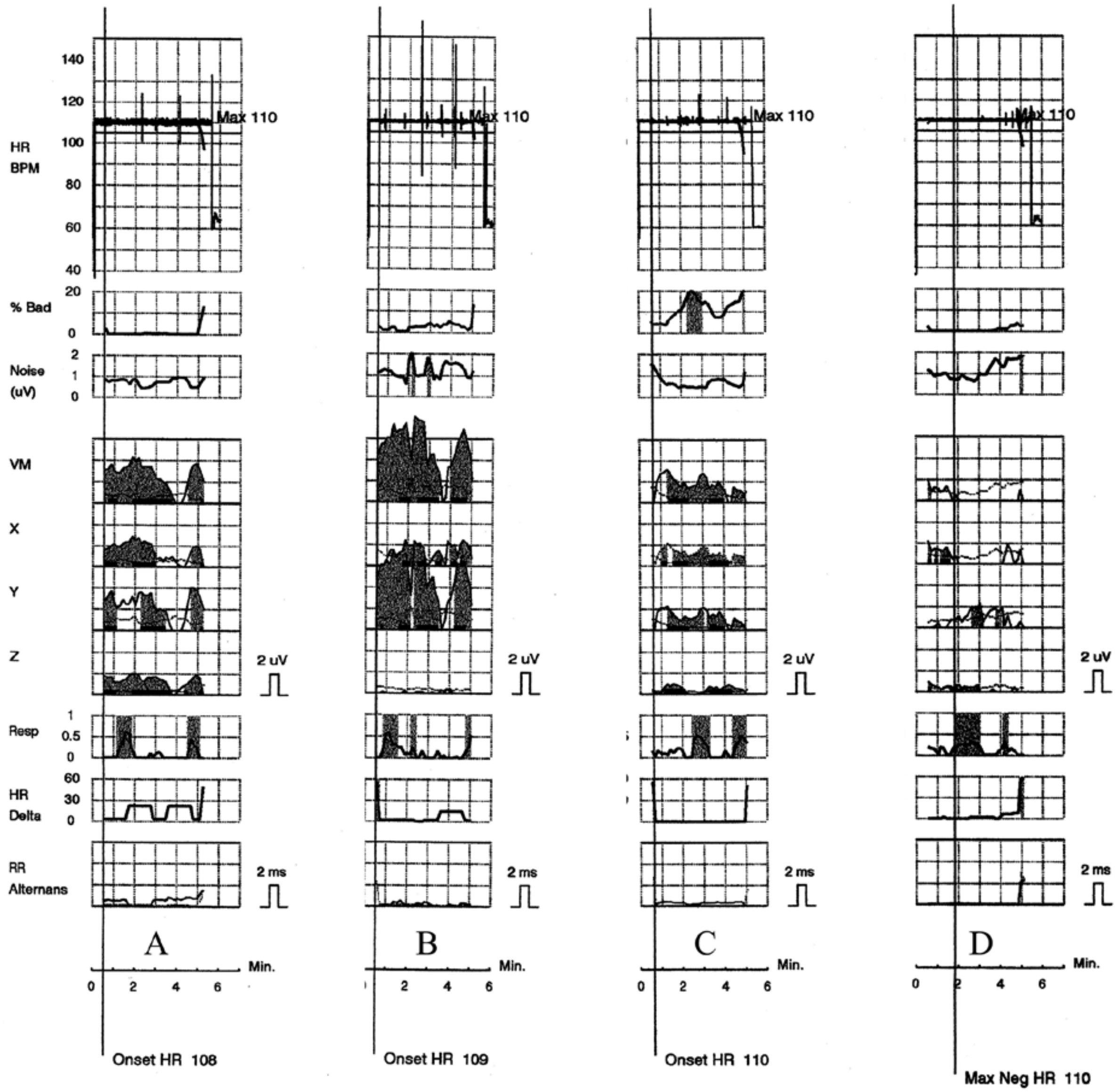

FIGURE 1. Microvolt T-wave alternans (MTWA) with the 4 different pacing modes in one patient. A= AAI mode, B=DDD mode, RV pacing, C= DDD mode, LV pacing, D= DDD mode, RV+LV pacing. LV = left ventric-le(-ular); RV = right ventric-le(-ular).

ventricular pacing correlates with MTWA during right atrial pacing and left ventricular pacing but did not correlate with MTWA during right ventricular pacing. This suggests that biventricular pacing does not have detrimental effects on the electrical milieu of the heart whereas; right ventricular pacing can be potentially proarrhythmic.

PREVIOUS STUDIES ON MTWA MEASUREMENT AND BIVENTRICULAR PACING

Ehrlich et al studied 30 patients who received cardiac resynchronization therapy. In their study there was a high level of concordance between MTWA test results during right atrial (RA) pacing, right ventricular (RV) pacing, left ventricular (LV) pacing and biventricular pacing. They concluded that biventricular pacing did not seem to affect the arrhythmogenic substrate as detected by MTWA testing.[9] The MTWA testing protocol included paced heart rates at 80, 90, 100, 110 beats/min with increments every 180 sec. On the other hand, Anh et al studied 33 patients who received cardiac resynchronization therapy. In their study, MTWA magnitude was lower during biventricular pacing compared to RA, RV or LV pacing. The MTWA protocol included pacing at 90, 100, 110, 120 beats/min, then 110, 100, 90 beats/min changing every 90 seconds. They concluded that biventricular pacing attenuates MTWA as compared to the other pacing modes. They also found that MTWA during RV pacing predicted arrhythmic events more effectively than MTWA with biventricular pacing or right atrial pacing.[8] From the study of Anh et al, it seems that biventricular pacing was superior to right atrial pacing unlike our study which showed that MTWA with biventricular pacing was comparable to atrial pacing.

Shalaby et al studied MTWA during atrial and ventricular pacing.[12] Although there was concordance between both tests, ventricular pacing generated higher amplitudes and noise and a higher percentage of nonnegative results. Similarly, in our study, patients with RV pacing were more likely to have a non-negative MTWA study.

STUDY LIMITATIONS

Microvolt T-wave alternans testing was performed on beta blockers and antiarrhythmic agents. There are conflicting data in the literature about the need to withhold beta blockers and antiarrhythmic agents prior to MTWA testing.[5,18-20] Nevertheless, patients served as their own control when they underwent MTWA testing during the different pacing modes.

We were not able to pace all the patients in the AAI mode because of their inability to conduct to the ventricle, or because of atrial fibrillation in some patients. The value of MTWA pacing in patients with atrial fibrillation who are paced from the ventricle is unknown.

CONCLUSIONS

Microvolt T-wave alternans during biventricular pacing correlates with MTWA during atrial pacing and left ventricular pacing and does not correlate with MTWA during right ventricular pacing in patients with congestive heart failure. Biventricular pacing has no detrimental effect on the electrical milieu of the ventricles.

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