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ORIGINAL ARTICLE

Microvolt T-wave alternans and other noninvasive predictors of serious arrhythmic events in patients with an implanted cardioverter-defibrillator

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Abstract

Background: Prediction of recurrent malignant ventricular tachyarrhythmias after insertion of a implantable cardioverter-defibrillator (ICD) is challenging. Microvolt T-wave alternans (MTWA) seems to be a promising marker of such events in ICD recipients.

Aim: To assess prognostic significance of MTWA and other noninvasive parameters in the prediction of major arrhythmic events after ICD implantation.

Methods: This prospective study included 155 patients (121 male, age 59 ± 11 years) in whom ICD was implanted for secondary prevention of a sudden cardiac death. In all patients, clinical evaluation along with estimation of ejection fraction, MTWA measurement using the HearTwave Cambridge Heart system, and determination of the corrected QT interval (QTc) and QT dispersion (QTd) based on resting ECG were performed 3 days before ICD implantation. Using 24-h Holter monitoring, cardiac arrhythmias, QT interval, QT dynamicity, QT variability (QTSD) and heart rate variability (HRV) time domain parameters were determined. MTWA results were categorised, based on the accepted criteria, as positive, negative or indeterminate. In further analyses, positive and indeterminate MTWA results were grouped together as abnormal or non-negative tests [MTWA(+)], while negative MTWA results were considered normal [MTWA(–)]. During the follow-up (mean duration 21.6 ± 11.6 months), major arrhythmic cardiac events (MACE), defined as death and/or the need for ablation and/or heart transplantation due to malignant ventricular tachyarrhythmias, were recorded.

Results: During the follow-up, MACE occurred in 17 (11%) patients. Abnormal MTWA before ICD implantation was found significantly more frequently in patients with MACE as compared to patients without MACE. Multivariate Cox regression analysis identified abnormal MTWA and QTSD as independent risk factors for MACE, with hazard ratios of 10.82 (95% CI 9.76–11.88; $p < 0.05$) and 1.08 (95% CI 1.05–1.08), respectively. Significant differences in MACE-free survival rate with regard to MTWA results (abnormal *vs* normal MTWA) were shown during the follow-up ($p < 0.001$). The negative predictive value of normal MTWA for MACE was 98.6%. When both MTWA and QTSD were combined, the positive predictive value increased to 35%, with a sensitivity of 82% and specificity of 81%. The probability of MACE with normal results of both these tests was 2.3%.

Conclusions: Abnormal MTWA is a strong independent predictor of MACE in ICD recipients, and QTSD is a weaker predictor. In the prediction of MACE after ICD implantation, the highest predictive value was noted for abnormal MTWA combined with QTSD. Normal values of these two parameters were associated with a low probability of MACE. These results suggest that standardised MTWA evaluation can be useful for risk stratification in the clinical practice.

Key words: microvolt T-wave alternans, implantable cardioverter-defibrillator, sudden cardiac death, ventricular arrhythmias, QT variability

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INTRODUCTION

During long-term follow-up after insertion of an implantable cardioverter-defibrillator (ICD) for the primary prevention of a sudden cardiac death (SCD), complex ventricular arrhythmia, including sustained ventricular tachycardia (VT) and ventricular fibrillation (VF) occur in about 30% of patients [1, 2], and recurrent ventricular tachyarrhythmia is noted in 50–70% of patients in the secondary prevention of SCD [3]. High-voltage ICD interventions terminate lethal ventricular arrhythmias but they are also associated with progression of chronic heart failure (CHF) and may lead to mortality due to the latter [2, 4]. In some patients, frequent recurrences of ventricular arrhythmia necessitating high-voltage ICD interventions occur despite optimal drug therapy, prompting ablation [5], or orthotopic heart transplantation (OHT) in case of progressive HF when other therapeutic options have failed.

Occurrence of major arrhythmic events after ICD implantation has prompted search for their noninvasive predictors. In addition to markers of the autonomic nervous system [6], microvolt T-wave alternans (MTWA) is a repolarisation-related predictor which is closely related to the occurrence of ventricular arrhythmia [7]. However, multicentre trials performed in the recent years, including ABCD and MASTER studies, yielded discordant results in regard to the utility of MTWA as a test to identify primary prevention patients in whom VT requiring high-energy ICD intervention will occur [8, 9]. In particular, this test did not identify patients at risk of the most serious arrhythmic events, occurring in about 5% of primary prevention ICD patients [10] and about 10–40% of secondary prevention patients [11]. Thus, the aim of our study was to evaluate prognostic values of MTWA and other noninvasive parameters as predictors of major arrhythmic events in patients with ICD.

METHODS

This prospective study included 155 patients who were selected, based on the study inclusion criteria, from a group of consecutive 162 patients who underwent ICD implantation for secondary prevention of SCD in 2003–2006, with indications for ICD implantation established using the European Society of Cardiology (ESC) guidelines [12, 13].

Due to the methodology used to measure MTWA, necessary inclusion criteria included [14]: (1) the presence of sinus rhythm, (2) lack of cardiac pacing, and (3) patient clinical condition allowing performance of an exercise test, with no concomitant disorders that would preclude it. The exclusion criteria included [14]: (1) the presence of permanent atrial fibrillation or flutter (4 patients), (2) cardiac pacing prior to ICD implantation (1 patient), and (3) inability to perform an exercise test (2 patients).

Ischaemic heart disease was diagnosed in 108 patients, non-ischaemic dilated cardiomyopathy in 37 patients, hypertrophic cardiomyopathy in 6 patients, and no organic heart disease was found in 4 patients. Clinical characteristics of the study population are shown in Table 1.

Table 1. Characteristics of the study population (n = 155)

Age [years]	59.8 ± 11.6
Male gender	121 (78.1%)
Hypertension	78 (50.3%)
Type 2 diabetes	33 (21.3%)
Previous anterior wall MI	51 (32.9%)
Previous inferior wall MI	53 (34.2%)
Cardiac disease aetiology:	
CHD	108 (69.7%)
Non-ischaemic CMP	37 (23.9%)
Other	10 (6.4%)
LVEF [%]	34.3 ± 11.6
NYHA class	1.9 ± 0.7
Beta-blocker	151 (97.4%)
Amiodarone	33 (21.3%)
ACEI	124 (80.0%)
Cause of ICD implantation:	
VF	62 (40.0%)
Haemodynamically unstable sVT	93 (60.0%)

MI — myocardial infarction; CHD — coronary heart disease; CMP — cardiomyopathy; LVEF — left ventricular ejection fraction; ACEI — angiotensin-converting enzyme inhibitor; ICD — implantable cardioverter-defibrillator; VF — ventricular fibrillation; sVT — sustained ventricular tachycardia

Routine non-invasive testing performed 3 days before ICD implantation included resting electrocardiogram (ECG), 24-h digital Holter monitoring and MTWA measurement. At the same time, New York Heart Association (NYHA) class was determined based on the clinical history, and echocardiographic biplane Simpson method was used to determine left ventricular ejection fraction (LVEF). In further analyses, LVEF ≤ 35% was considered to be associated with an increased risk of SCD [2].

MTWA measurement

MTWA was measured during a treadmill exercise test using the HearTwave system (Cambridge Heart Inc, Bedford, Massachusetts, USA) in patients receiving their chronic drug therapy. MTWA measurement result was categorised as positive, negative, or indeterminate [15]. Positive MTWA test was defined as the presence of sustained alternans (lasting for at least 1 min, with amplitude of ≥ 1.9 μV and the ratio of ≥ 3) appearing at the heart rate of ≤ 110 bpm. MTWA test result was categorised as negative when conditions of a positive result were not met and maximum negative heart rate was ≥ 105 bpm. MTWA test result was categorised as indeterminate if it was neither positive nor negative. In further analyses, negative MTWA results were considered normal [MTWA(–)],

and positive and indeterminate MTWA results were grouped together as abnormal [MTWA(+)] [14–16], also called non-negative by some authors [9]. All automatic results were verified by a researcher present throughout the test.

Evaluation of other noninvasive risk factors

Resting 12-lead ECG (at 50 mm/s). We measured QT interval and corrected QT interval (QTc) [ms] using the Bazett formula in lead II, and QT dispersion (QTd) [ms] as the difference between the maximum and minimum QT interval.

24-hour digital Holter monitoring. We performed quantitative and qualitative analysis of arrhythmia, including the number of ventricular extrasystole (VE), nonsustained ventricular tachycardia (NSVT), and sustained ventricular tachycardia (sVT). We also measured QT parameters: QT interval, maximum duration of QT interval (QTmax) [ms], QRS onset to the peak of T wave interval (QTa) [ms], maximum duration of QRS onset to the peak of T wave interval (QTamax) [ms], and QT interval variability defined as standard deviation of all QT intervals (QTSD) [ms].

We evaluated QT dynamicity based on the slope of linear regression curve during 24 h (Sa), daytime (Sd), night-time (Sn), and morning hours (Sm). We also evaluated heart rate variability (HRV) by measuring the following parameters: standard deviation of all sinus rhythm RR intervals (SDNN) [ms], and the triangular index (TI), defined as the ratio of the base and the height of RR interval histogram triangle.

Measurements of QT interval, dynamicity, and variability reflect repolarisation, and HRV parameters reflect autonomic nervous system function.

For markers with threshold values reported in the ESC guidelines or documented in multicentre studies to correlate with increased SCD risk, the following established values were used [6, 13]: LVEF ≤ 35%, VE > 10/h, QTc > 440 ms, QTd > 60 ms, SDNN < 70 ms, and TI < 25.

Long-term follow-up

Mean duration of follow-up after ICD implantation was 21.6 ± 11.6 months. During this long-term follow-up, we recorded the occurrence of major arrhythmic cardiac events (MACE), defined as death due to any cause and/or the need for ablation due to malignant ventricular tachyarrhythmias and/or OHT due to malignant ventricular tachyarrhythmias when other therapeutic options have failed.

Statistical methods

Results are expressed as mean values ± SD or numbers and percentages. Continuous variables were compared using the Student t-test, and categorical variables using the χ^2 test. Independent risk factors of the primary endpoint were identified in a multivariate Cox regression analysis including all variables that differed between the groups. Results of the latter analysis are shown as hazard ratios (HR) and 95% confidence intervals (CI). Differences in the primary endpoint rate depending on the result of particular tests are shown using cumulative Kaplan-Meier curves, and significance of these differences was evaluated using the log-rank test. Due to lack of established normal values of some parameters evaluated in our study, cut-off points defined as the median values in the overall study population were used to estimate the diagnostic accuracy of independent risk factors of the primary endpoint, including their positive (PPV) and negative predictive value (NPV), sensitivity, and specificity. A p value < 0.05 was considered statistically significant. Statistical analyses were performed using the STATISTICA 6.0 software (StatSoft Inc., Tulsa, OK, USA).

RESULTS

Overall, abnormal MTWA was noted in 82 (52.9%) patients, including a positive result in 52 (33.5%) patients and an indeterminate result in 30 (19.4%) patients. In the remaining 73 (47.1%) patients, MTWA was normal.

Long-term follow-up

Total mortality was 1.9% and consisted of 3 cardiac deaths, including one categorised as an arrhythmic SCD according to the definition by Hinkle and Thaler [17]. Five patients were referred for OHT due to frequent recurrences of ventricular arrhythmia that was intractable despite frequent treatment modifications, including episodes of electrical storm with concomitant progressive CHF in 3 patients. In 14 patients, radiofrequency ablation was performed due to recurrent ventricular arrhythmia and electrical storms leading to frequent ICD therapies despite drug treatment modifications and optimization of antiarrhythmic ICD intervention protocols. Among patients who died, one underwent ablation and one underwent OHT due to reasons described above. In addition, ablation was performed in 3 patients referred for OHT. Thus, the group with MACE included 17 (11%) patients. Before referral for both OHT and ablation, optimal myocardial revascularisation was performed in patients with ischaemic aetiology of the arrhythmia.

Comparison of patients with or without MACE

Patients with MACE were older, more frequently male, and more frequently with a history of hypertension, diabetes, previous anterior wall myocardial infarction, ischaemic heart disease and higher NYHA class. However, these differences were not statistically significant. The two groups also did not differ in regard to other clinical characteristics and drug therapy used (Table 2). We also did not find any significant differences between patients with or without MACE in regard to the cause of ICD implantation, i.e. history of VF or haemodynamically unstable sVT (Table 2).

Mean LVEF did not differ between the two groups. Among patients with MACE, insignificantly higher proportions of pa-

Table 2. Comparison of demographic and clinical data between patients with or without a major arrhythmic cardiac event (MACE)

	With MACE (n = 17)	Without MACE (n = 138)	P
Age [years]	63.8 ± 8.8	59.3 ± 11.8	NS
Male gender	15 (88.2%)	106 (76.8%)	NS
Hypertension	11 (64.7%)	67 (48.6%)	NS
Type 2 diabetes	6 (35.3%)	27 (19.6%)	NS
Previous anterior wall MI	8 (47.1%)	43 (31.2%)	NS
Previous inferior wall MI	5 (29.4%)	48 (34.8%)	NS
Cardiac disease aetiology:			
CHD	14 (82.4%)	94 (68.1%)	NS
Non-ischaemic CMP	3 (17.6%)	34 (24.6%)	NS
Other	0 (0.0%)	10 (7.2%)	NS
NYHA class	2.2 ± 0.7	1.8 ± 0.7	NS
Beta-blocker	16 (94.1%)	135 (97.8%)	NS
Amiodarone	4 (23.5%)	29 (21.0%)	NS
ACEI	14 (82.4%)	110 (79.7%)	NS
VF	9 (52.9%)	53 (38.4%)	NS
Haemodynamically unstable sVT	8 (47.1%)	85 (61.6%)	NS

Abbreviations as in Table 1

tients with LVEF ≤ 35% and VE > 10/h were noted. We did not find more frequent occurrences of NSVT in patients with MACE (Table 3). Abnormal MTWA was significantly more common in the MACE group. These patients were also characterised by significantly prolonged QTc and significantly more frequent QTc prolongation > 440 ms. QTd and the proportion of patients with QTd > 60 ms were also significantly higher. In contrast, HRV parameters were significantly lower, and the proportions of patients with TI < 25 and SDNN < 70 ms were higher. We did not find any significant differences between patients with or without MACE in regard to QT parameters in Holter monitoring and QT dynamicity. Finally, QTSD was significantly higher in patients with MACE (Table 3).

Independent risk factors for MACE

Multivariate Cox regression analysis showed that abnormal MTWA and QTSD were independent risk factors for MACE. Abnormal MTWA was associated with an 11-fold increased risk of MACE, and every 1 ms increase in QTSD was associated with an 8% increase in the risk of MACE (Fig. 1). Due to lack of a universally accepted threshold value of QTSD as a risk factor for SCD, it was treated as a continuous variable in our comparative analysis.

Differences in the occurrence of MACE depending on the results obtained for specific predictors

Significant differences in the occurrence of MACE during the long-term follow-up depending on the result of MTWA test, QTSD, and MTWA combined with QTSD, were shown using Kaplan-Meier curves. The largest difference in the occurrence of MACE was illustrated by the curve showing combined MTWA and QTSD analysis (Fig. 2).

Assessment of the prognostic value of independent risk factors for MACE

For abnormal MTWA and QTSD results, we performed additional analyses to determine their prognostic value in predicting MACE. Due to lack of a universally accepted threshold value of QTSD as a risk factor for SCD, the cut-off value was defined as the median value in our study population (30 ms). PPV for MTWA and QTSD were comparable and increased when the two predictors were analysed jointly. A high NPV was found for both predictors, and the highest value was observed for MTWA (98.6%). Both were also highly sensitive, but we found that only MTWA combined with QTSD was characterised by a high sensitivity and an acceptable specificity. The probability of MACE with normal results of both these tests was 2.3% (Table 4).

DISCUSSION

The most important finding of our study was that abnormal MTWA was demonstrated to be an independent risk factor for MACE following ICD implantation, defined as death, need for ablation due to recurrent ventricular tachyarrhythmias, or OHT when other therapeutic options have failed.

Two previous metaanalyses, one including 19 prospective studies on primary and secondary SCD prevention, and the other including only 8 primary prevention studies, sho-

Table 3. Comparison of the analyzed parameters between patients with or without a major arrhythmic cardiac event (MACE)

	With MACE (n = 17)	Without MACE (n = 138)	P
LVEF [%]	31.0 ± 8.6	34.7 ± 11.9	NS
LVEF ≤ 35%	13 (76.5%)	80 (58.0%)	NS
VE > 10/h	9 (52.9%)	47 (34.1%)	NS
NSVT	4 (23.5%)	27 (19.6%)	NS
MTWA(+)	16 (94.1%)	66 (47.8%)	< 0.001
QTc [ms]	462.6 ± 24.4	447.3 ± 23.4	< 0.05
QTc > 440 ms	13 (76.5%)	70 (50.7%)	< 0.05
QTd [ms]	62.4 ± 9.2	57.3 ± 9.2	< 0.05
QTd > 60 ms	12 (70.6%)	51 (37.0%)	< 0.05
QT [ms]	432.2 ± 41.2	424.1 ± 37.4	NS
QTmax [ms]	475.6 ± 49.8	460.5 ± 42.6	NS
QTa [ms]	350.5 ± 37.3	340.0 ± 31.6	NS
QTamax [ms]	389.9 ± 42.0	375.4 ± 37.6	NS
QTSD [ms]	37.1 ± 6.8	29.4 ± 7.5	< 0.001
QTSD ≥ 30 ms	14 (82.4%)	55 (39.9%)	< 0.001
Sa	0.205 ± 0.07	0.188 ± 0.08	NS
Sd	0.178 ± 0.05	0.170 ± 0.07	NS
Sn	0.170 ± 0.07	0.154 ± 0.13	NS
Sm	0.209 ± 0.05	0.189 ± 0.06	NS
TI	18.1± 5.4	21.7 ± 6.1	< 0.05
TI < 25	15 (88.2%)	82 (59.4%)	< 0.05
SDNN [ms]	87.7 ± 21.5	103.2 ± 24.8	< 0.05
SDNN < 70 ms	6 (35.3%)	10 (7.2%)	< 0.001

LVEF — left ventricular ejection fraction; VE — ventricular extrasystole; NSVT — nonsustained ventricular tachycardia; MTWA(+) — abnormal microvolt T-wave alternans; QTc — corrected QT interval; QTd — QT dispersion; Holter monitoring QT interval parameters: QT, QTmax, QTa, QTamax; QTSD — QT variability; QT dynamicity parameters: Sa, Sd, Sn, Sm; Heart rate variability parameters: TI, SDNN

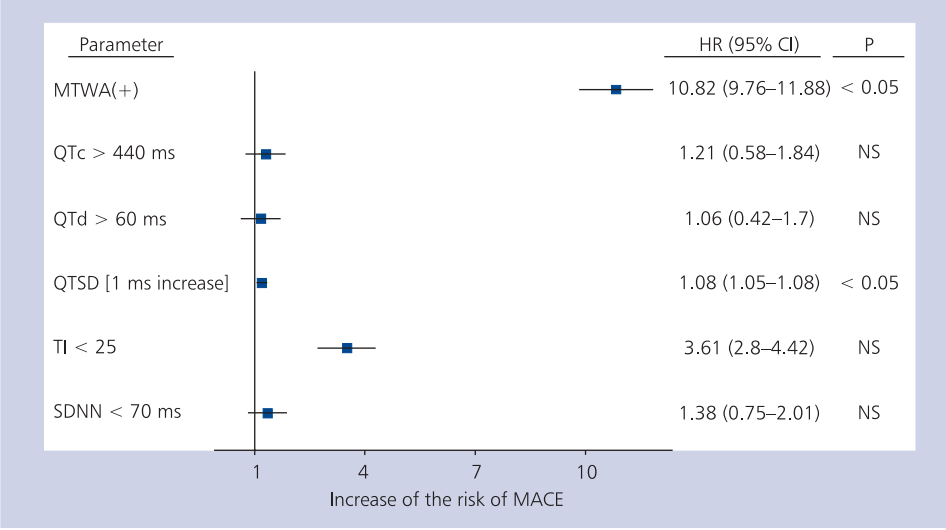

Figure 1. Multivariate analysis including parameters that potentially affected the occurrence of major arrhythmic cardiac events (MACE); MTWA(+) — abnormal microvolt T-wave alternans; QTc — corrected QT interval; QTd — QT dispersion; QTSD — QT variability; TI, SDNN — parameters of heart rate variability; HR — hazard ratio; CI — confidence interval

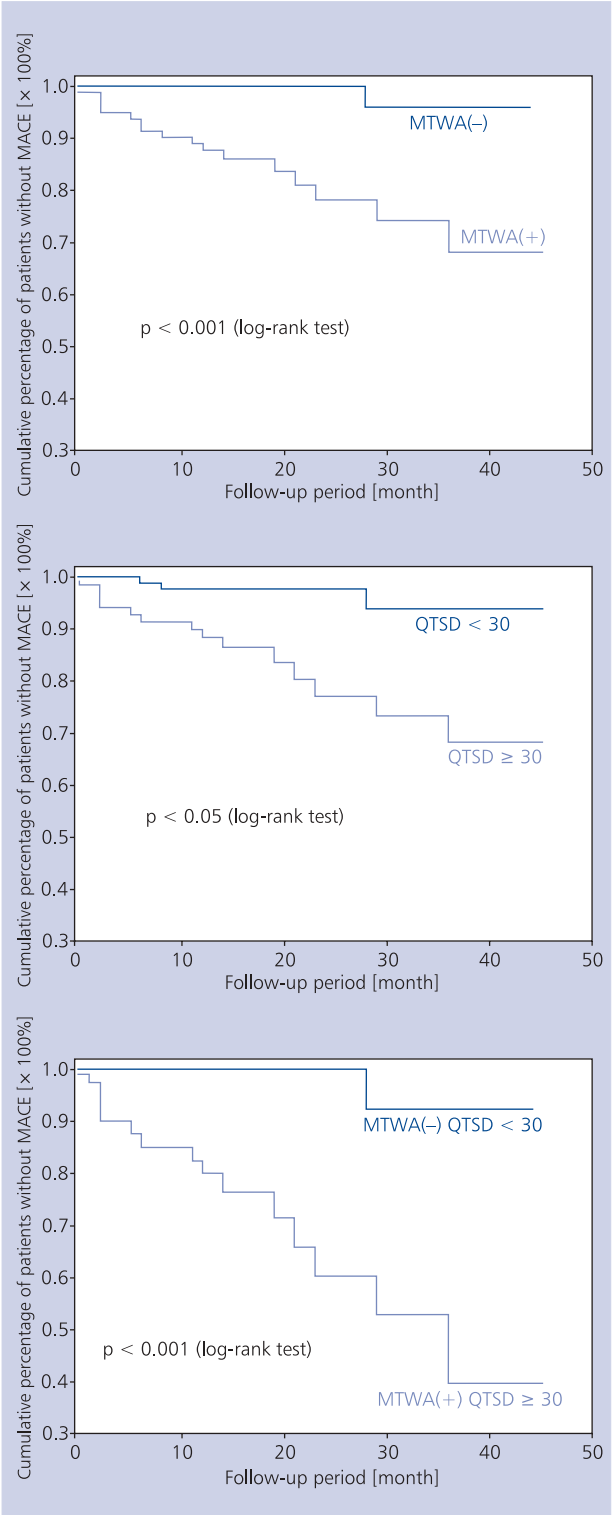

Figure 2. Kaplan-Meier curves showing differences in the occurrence of major arrhythmic cardiac events (MACE) during the long-term follow-up depending on the result of MTWA and/or QTSD evaluation; MTWA(+) — abnormal microvolt T-wave alternans; MTWA(–) — normal microvolt T-wave alternans; QTSD — QT variability

wed that abnormal MTWA was associated with a 3-fold increased risk of SCD, VF and sVT, and more than two-fold increased risk of mortality due to malignant ventricular arrhythmia [18, 19]. However, the endpoints evaluated in these studies were not defined in the same way as MACE in our study. With current wider availability of ICD to prevent SCD, it is particularly important to define patients at the highest risk of recurrent malignant ventricular arrhythmia. If drug therapy fails, ablation should be performed in such patients. Our findings indicate that MTWA may be useful in the identification of such patients.

Recent study findings, including the randomised ABCD study which showed that compared to invasive electrophysiological studies, MTWA has a similar diagnostic value in predicting arrhythmic event in the primary prevention of SCD [8], and the 2005 metaanalysis mentioned above, led to the use of MTWA in such patients becoming a class IIa recommendation, level of evidence A, in the international guidelines on ventricular arrhythmia and SCD [13]. This means that this test is now considered justified as a diagnostic method and risk stratification tool in patients at risk of malignant ventricular arrhythmia [13]. Our findings confirm the prognostic value of MTWA, negating results of two other randomised studies, MASTER [9] and CARISMA [20]. The former did not confirm a relationship between abnormal MTWA and arrhythmic events after ICD implantation for primary prevention in a MADIT II study population, and the latter failed to show that MTWA was an independent risk factor for malignant ventricular arrhythmia. In both studies, varying methods were used to evaluate MTWA, including cardiac pacing or dobutamine infusion used during the testing in a major proportion of patients which may have significantly affected the reported findings. It has been stressed that the most physiological approach to evaluate MTWA is testing during exercise and the methodology used should be standardised [21]. Our study has complied with these recommendations regarding MTWA evaluation.

Another independent risk factor for major arrhythmic events is QTSD. In the recent years, it has been noted that increased QTSD is associated with an increased risk of SCD [22]. In our study, combining MTWA assessment with increased QTSD resulted in better patient stratification compared to each of these predictors by itself. This promising parameter, which has been shown to predict appropriate ICD interventions in the MADIT II study population [23], has not been included in the guidelines yet. The highest sensitivity and specificity of combined evaluation of MTWA and QTSD found in our study confirms the usefulness of this approach of combining markers to increase their prognostic value.

Numerous studies highlighted a very high NPV of a negative MTWA result, in the range of 94–100% [24, 25]. In the ABCD study, arrhythmic events occurred in only 2% of pa-

Table 4. Prognostic value, sensitivity, and specificity of independent predictors of major arrhythmic cardiac events

	PPV	NPV	Sensitivity	Specificity	HR	P
MTWA(+)	0.195	0.986	0.941	0.522	16.26	< 0.05
QTSD ≥ 30	0.203	0.965	0.824	0.601	6.04	< 0.05
MTWA(+) QTSD ≥ 30	0.350	0.974	0.824	0.812	16.92	< 0.001
MTWA(–) QTSD < 30	0.023	0.856	0.059	0.688	0.16	0.07

MTWA(+) — abnormal microvolt T-wave alternans; QTSD ≥ 30 — QT variability ≥ 30 ms; MTWA(+) QTSD ≥ 30 — abnormal microvolt T-wave alternans with QT variability ≥ 30 ms; MTWA(–) QTSD < 30 — normal microvolt T-wave alternans with QT variability < 30 ms; PPV — positive predictive value; NPV — negative predictive value; HR — hazard ratio

tients with negative results of both MTWA testing and the electrophysiological study [8]. Our study findings also indicate a high NPV of MTWA, particularly when combined with QTSD, as with normal values of both these tests, the likelihood of MACE was only 2.3%.

Our results may be of a significant importance in the clinical practice. Using MTWA to identify patients at the highest risk of arrhythmic events following ICD implantation underscores the need for optimal drug therapy, or even considering arrhythmia substrate ablation before ICD implantation, as suggested by some recent studies including SMASH-VT [26].

Limitations of the study

Due to the methodology used to evaluate MTWA, our study group did not include patients with permanent atrial fibrillation which precluded MTWA-based risk stratification using this approach. In our study, MTWA testing was performed without discontinuing chronic drug therapy, including beta-blockers, which resulted in some indeterminate MTWA results but the proportion of such results was not increased compared to the literature data. Similarly, we did not withhold amiodarone which may reduce the number of positive MTWA results [27]. This drug was used for the treatment of symptomatic complex ventricular arrhythmia in more than 20% of our patients, without significant differences between patients with and without MACE, and thus likely exerted a similar effect on the results in both groups. Amiodarone therapy was stopped in most patients after ICD implantation. The ABCD study showed that the predictive value of MTWA diminished after 12 months of follow-up and thus it has been suggested that such testing should be repeated every 1–2 years [28].

CONCLUSIONS

Abnormal MTWA is a strong independent predictor of MACE in ICD recipients. Another weaker predictor is QTSD. The highest predictive value in the prediction of MACE after ICD implantation was noted for abnormal MTWA combined with QTSD. Normal values of these two parameters were associated with a low probability of MACE. Standardisation of MTWA evaluation allows its use for risk stratification in the clinical practice.

Conflict of interest: *Beata Średniawa is a consultant for Medtronic Bakken Research Centre, Oskar Kowalski is a consultant for Biotronik and Medtronic, and Radosław Lenarczyk is a consultant for Biotronik and Medtronic. Conflict of interest of remaining authors: none declared.*

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Mikrowoltowa naprzemienność załamka T i inne nieinwazyjne wskaźniki przewidywania poważnych zdarzeń arytmicznych u chorych z wszczepionym kardiowerterem-defibrylatorem

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Streszczenie

Wstęp: Wskaźniki przewidywania nawrotów złożonych arytmii komorowych po wszczepieniu kardiowertera-defibrylatora (ICD) są mało poznane. Wyniki badań z ostatnich lat, mimo pewnych rozbieżności, wskazują na przydatność mikrowoltowej naprzemienności załamka T (MTWA) w prognozowaniu zdarzeń arytmicznych po wszczepieniu ICD.

Cel: Celem pracy była ocena wartości prognostycznej MTWA i innych nieinwazyjnych predyktorów w przewidywaniu poważnych zdarzeń arytmicznych u chorych z ICD.

Metody: Badaniem prospektywnym objęto 155 osób (121 mężczyzn; śr. wiek 59 ± 11 lat) z ICD wszczepionym w ramach profilaktyki wtórnej nagłego zgonu sercowego. U wszystkich chorych 3 dni przed implantacją ICD oceniono stan kliniczny, frakcję wyrzutową lewej komory oraz MTWA, stosując system HearTwave Cambridge Heart, USA. Na podstawie spoczynkowego zapisu EKG obliczono skorygowany odstęp QT (QTc) i dyspersję QT (QTd). W 24-godzinnym badaniu holterowskim oceniono zaburzenia rytmu serca, odstęp QT, dynamikę QT i zmienność QT (QTSD) oraz czasowe parametry zmienności rytmu zatokowego (HRV). Wynik MTWA klasyfikowano jako dodatni, ujemny i nieokreślony na podstawie powszechnie akceptowanych kryteriów. W dalszych analizach wynik testu MTWA: dodatni i nieokreślony traktowano łącznie jako nieprawidłowy wynik testu [MTWA(+)], nazywany także nie-ujemnym, a wynik ujemny jako prawidłowy wynik testu [MTWA(–)]. Średni czas obserwacji wynosił 21,6 ± 11,6 miesiąca, w czasie którego odnotowywano poważne sercowe zdarzenia arytmiczne [MACE: zgon z jakiejkolwiek przyczyny i/lub wykonanie ablacji z powodu złośliwej arytmii komorowej, i/lub transplantacja serca (OHT) z powodu złośliwego charakteru arytmii komorowej po wyczerpaniu możliwości terapeutycznych].

Wyniki: Podczas średnio 21-miesięcznej obserwacji MACE wystąpiły u 17 (11%) osób, w tym 3 zgony sercowe. U pacjentów z MACE w porównaniu z osobami bez MACE istotnie częściej wystąpił nieprawidłowy wynik testu MTWA (94,1% *v.* 47,8%; $p < 0,001$). Ponadto pacjentów z MACE i bez MACE różnicowały istotnie: dłuższy czas trwania QTc, zwiększona QTd, zwiększona QTSD i obniżone parametry HRV. W analizie wieloczynnikowej wykazano, że niezależnymi czynnikami ryzyka wystąpienia MACE był nieprawidłowy wynik testu MTWA, zwiększający ryzyko 11-krotnie (95% CI 9,76–11,88; $p < 0,05$), oraz zwiększona QTSD, której wzrost o 1 ms powodował zwiększenie ryzyka o 8% (95% CI 1,05–1,08; $p < 0,05$). Obserwowano także znamienne różnice w wystąpieniu MACE w obserwacji odległej, w zależności od prawidłowego i nieprawidłowego wyniku testu MTWA ($p < 0,001$). Siła przewidywania negatywnego (NPV) dla MTWA wynosiła 98,6%. Przy połączeniu obu markerów siła przewidywania pozytywnego (PPV) wzrastała do 35%, przy 82% czułości i 81% swoistości. W przypadku prawidłowych wyników obu markerów prawdopodobieństwo wystąpienia MACE było równe 2,3%.

Wnioski: Nieprawidłowy wynik testu MTWA jest silnym niezależnym czynnikiem ryzyka poważnych zdarzeń arytmicznych po wszczepieniu ICD. Innym słabszym markerem jest QTSD. W przewidywaniu MACE po wszczepieniu ICD najwyższą siłę predykcyjną ma nieprawidłowy wynik testu MTWA oceniany łącznie ze zwiększoną QTSD. Przy obu prawidłowych wynikach prawdopodobieństwo wystąpienia tych zdarzeń w obserwacji długoterminowej jest niskie. Standaryzacja badania MTWA pozwala na jego wykorzystanie w stratyfikacji ryzyka zdarzeń arytmicznych w warunkach klinicznych.

Słowa kluczowe: mikrowoltowy alternans załamka T, kardiowerter-defibrylator, nagły zgon sercowy, arytmie komorowe, zmienność QT

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