Is T-Wave Alternans Testing Feasible in Candidates for Prophylactic Implantable Defibrillators?

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Abstract

Aims Previous studies have demonstrated that microvolt T-wave alternans (TWA) screening in patients with ischaemic and dilated cardiomyopathy is effective in identifying patients at high or low risk of sudden cardiac death. It remains unclear which percentage of potential recipients of an implantable cardioverter defibrillator (ICD) are able to perform TWA testing using an exercise protocol which is, at this moment, the golden standard. In this study, we evaluated the feasibility of TWA in the risk stratification of potential ICD recipients with ischaemic or dilated cardiomyopathy.

Methods and Results Medical charts of 165 primary prevention ICD recipients were reviewed to decide if patients were able to perform a TWA exercise test or not. Reasons to waive a test were: atrial fibrillation or flutter, pacemaker dependency, recent (cardiovascular) surgery (<1 month) and inability to exercise. Of the potential ICD recipients 35% had one or more of these contraindications and were therefore not suitable for testing.

Conclusion In several studies, TWA is a promising risk stratifier for predicting sudden cardiac death; however, in our population, 35% of the potential ICD candidates could not be

tested. In order to fulfil its promise as a predictor for SCD, an alternative means to measure TWA needs to be evaluated.

Keywords Microvolt T-wave alternans · Implantable cardioverter defibrillator · Risk stratification · Ischemic cardiomyopathy · Dilated cardiomyopathy

Introduction

Sudden cardiac death (SCD) is the most common cause of death in the Western world [1]. With the introduction of the implantable cardioverter defibrillator (ICD), patients can be protected against SCD due to ventricular arrhythmia (VA). Primary prevention ICD trials demonstrated that patients with a reduced left ventricular ejection fraction will benefit from ICD implantation when compared with optimal medical treatment alone [2, 3]. However, given the fact that most ICD recipients will never experience a life-threatening VA, requiring antitachycardia pacing or shock therapy, better risk stratification is desirable to reduce the number of unnecessary device implantations.

Previous studies have demonstrated that microvolt T-wave alternans (TWA) screening in patients with ischaemic and dilated cardiomyopathy (CMP) is effective in identifying patients at high or low risk for SCD or all-cause mortality [4–6]. In the current ACC/AHA/ESC guidelines for management of patients with VA and the prevention of SCD, there is a class IIa indication for TWA testing to improve the diagnosis and risk stratification in patients with ischaemic and dilated CMP [7]. TWA is a heart rate-dependent measurement of subtle beat-to-beat changes in the amplitude of the T-wave, probably reflecting temporal heterogeneity or dispersion in ventricular repolarisation and predisposing patients to re-entry VA [8]. However, one of the limitations

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of TWA testing is that it is not feasible in every patient. For example, patients with atrial fibrillation or inability to exercise cannot be examined. In most TWA studies, these patients are excluded. It remains unknown which percentage of potential ICD recipients, in a real-life population, is eligible for TWA testing using an exercise protocol.

In this study, we evaluated the feasibility of TWA testing using the exercise protocol in the risk stratification of potential ICD recipients in a real-life population.

Methods

Study Population

Patients with ischaemic or dilated CMP receiving a prophylactic ICD (primary prevention) following current guidelines in the Medisch Spectrum Twente, Enschede, the Netherlands, between 1 January 2008 and 31 May 2009 were included in the analysis [7]. Reviewing the medical charts, it was decided whether a patient was eligible for TWA testing using the exercise protocol or not.

Using the exercise protocol, patients have to increase their heart rate while cycling. After gradually increasing the workload, a constant heart rate between 100 and 110 beats/min for 2.5 min has to be achieved, followed by a constant heart rate between 110 and 120 for 1.5 min.

Reasons to waiver a TWA test were (1) atrial fibrillation or atrial flutter at the moment of implantation, (2) a paced ventricular rhythm, (3) recent (cardiovascular) surgery (less than 1 month because of potential sternum instability) and (4) the inability to perform exercise due to heart failure or comorbidities [9, 10]. The aim of our analysis is to determine the number of patients not able to perform a TWA test due to these patient-related factors.

Statistical Analysis

Statistical analyses were performed with SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as a mean $\pm$ SD, and categorical data are summarised as frequencies and percentages. Differences in baseline characteristics between groups were analysed using Student's *t* tests and χ^2 tests or Fisher's exact test, as appropriate. To construct a prediction model for the ability to perform a TWA test, a multiple logistic regression was done. All tests were two-sided and $P < 0.05$ was considered statistically significant.

Results

Between 1 January 2008 and 31 May 2009, 165 patients with ischaemic or dilated CMP received an ICD for primary

prevention and were therefore candidates for pre-implantation TWA testing.

Feasibility for TWA Testing

A review of the charts identified 58 patients (35%) who were not suitable for TWA testing using an exercise protocol: 35 were excluded due to atrial fibrillation, 13 due to recent surgery, six due to comorbidity (two in NYHA class IV, two with third-degree atrioventricular block without pacemaker, one with a ventricular bigeminy, and one with inability to sit on a saddle because of an anal fistula), and four patients due to pacemaker dependency. Patient characteristics of both groups can be found in Table 1.

Discussion

TWA is a heart rate-dependent measurement of subtle changes in the amplitude of the T-wave, which occur every alternate beat. TWA probably reflects temporal heterogeneity or dispersion in ventricular repolarisation, which can lead to

Table 1 Patient characteristic for patients eligible and not eligible for TWA testing using an exercise protocol

	All patients	Eligible	Not eligible
Patients	165	107	57
Men/Women	138/27	88/19	49/8
Age, years ($\pm$ SD)	63.6 (10.2)	62.2 (10.6)	66.2 (9.0)
Aetiology			
Ischaemic	102 (62)	64 (60)	38 (66)
Dilated	63 (38)	43 (40)	20 (34)
Comorbidities			
COPD	19 (12)	12 (11)	7 (13)
DM	41 (25)	22 (21)	19 (33)
CVA	7 (4)	0 (0)	7 (13)
Recent surgery	13 (8)	0 (0)	13 (22)
AF			
Chronic	23 (14)	0 (0)	23 (40)
Paroxysmal	21 (13)	6 (6)	15 (26)
NYHA class			
I	6 (4)	5 (5)	1 (2)
II	84 (51)	68 (64)	16 (28)
III	62 (37)	30 (28)	32 (55)
IV	1 (1)	0 (0)	1 (2)
Unknown	11 (7)	4 (3)	7 (13)

All values are in numbers (percentage) unless otherwise specified
COPD chronic obstructive pulmonary disease, *DM* diabetes mellitus, *CVA* cerebral vascular accident, *AF* atrial fibrillation, *NYHA* New York Heart Association

P values are for univariate (p_u) and multivariate (p_m) analysis

formation of re-entry circuits and therefore lead to VA [8]. Especially the high-negative predictive value (>90%) makes it a valuable tool for identification of a group of patients who will probably not benefit from ICD implantation [4]. However, using the golden standard, the exercise protocol, to assess TWA, our study suggests that a substantial percentage of ICD candidates cannot be tested (35%).

Given the large percentage of patients not suitable for assessment, other protocols to measure TWA may be useful. Besides using an exercise protocol, TWA using the spectral analysis can also be estimated by pacing or by pharmacological testing.

Using pacing, two pacing modes can be used: atrial and atrioventricular pacing. During atrial pacing, the depolarisation and repolarisation of the ventricles will not differ from exercise, but this method cannot be used in patients with atrial fibrillation and patients with an AV block. Concordance rates between exercise testing and atrial pacing are reported to be between 55% and 81% [11–14]. Its prognostic value was studied by Rashba et al. [13] who found no prognostic value for incidence of death, sustained VA, and appropriate ICD therapy using an atrial paced protocol. Using a ventricular pacing protocol, patients with atrial fibrillation and AV block can be tested as well. A concordance of 57–79% between exercise testing and atrioventricular pacing was found [11, 14], and a concordance of 83% between right atrial and right ventricular pacing. There is no literature available pertaining to the prognostic significance of a positive TWA test performed by ventricular pacing protocols. A possible explanation for the differences between outcome of exercise and pacing TWA is the obvious difference in the level of adrenergic stimulation. A possible hypothesis is that adrenalin has, through stimulation of the IKS channel, a marked influence on the action potential duration, and therefore on the repolarisation of cardiac muscle, which can reflect in the occurrence of TWA [15].

In the pharmacological protocol, atropine is used to raise the heart rate. This method is not useful for patients with atrial fibrillation or an AV block. Failure to achieve the target heart rate occurs in 18% of the patients. Concordance (compared with right atrial pacing) was 96% [16]. No literature seems to be available on the concordance with exercise or, even more important, its prognostic value.

Another method to assess TWA is the modified moving average analysis (MMA) of TWA. This TWA analysis measures beat-to-beat variation in T-wave amplitude using data from a 24-h Holter. Using MMA–TWA, it is possible to assess TWA without controlling heart rate [17]. In patients with left ventricular dysfunction, positive MMA–TWA is predictive of cardiac mortality [18]. In patients with irregular rhythms (e.g. atrial fibrillation or frequent extrasystoles), data analysis is not possible and MMA–TWA measurement in these patients is not useful.

In patients without atrial fibrillation or inability to exercise, TWA measurement with the exercise protocol is the first choice. In patients with inability to exercise or in patients with indeterminate test results due to failure to reach the target heart rate, the atrial paced protocol is an option. In patients with atrial fibrillation or other irregular rhythms, TWA testing cannot be performed using nowadays techniques.

Limitations of our study include the retrospective design, and the single-centre experience. Reviewing of the medical records on certain criteria which are associated with a likely inability to perform an exercise test or with inability to analyse TWA data only gives an estimation of the feasibility of TWA testing.

Conclusion

In several studies, TWA testing is a promising risk stratifier for predicting sudden cardiac death. Unfortunately, in our population, a substantial percentage of the potential ICD candidates cannot be tested (35%). In order to fulfil its promise as a predictor for SCD, alternative means to measure TWA should be evaluated.

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