

The prognostic value of T-peak T-end among patients with implantable cardiac defibrillator for secondary prevention

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Abstract

Aim: Cardiac death due to ventricular arrhythmias can occur in patients with ICD (implantable cardioverter defibrillator) for secondary prevention. The aim of this study is to assess the prognostic value of electrocardiographic ventricular repolarization parameters in patients with secondary prevention.

Materials and Methods: Sixty five patients with ICD for secondary prevention after sustained ventricular tachycardia, ventricular fibrillation or sudden cardiac death were enrolled to the study retrospectively. Patients were divided into groups according to mortality during a follow up period of 4,5 years (48 patients alive and 17 dead). Heart rate, QT, QTc and T peak T end (Tp-e) duration were measured from 12 derivations ECG electronically.

Results: Mean age of the study population was 70.6 ± 11.9 years. Ventricular repolarization parameters such as QT, QTc, Tp-e duration and Tp-e index values were found to be similar between deaths and live patient groups. Patients who died during the follow-up had advanced age (68.7 ± 12.5 vs 76.8 ± 10.3 years, $p=0.009$), lower left ventricular ejection fraction percentage (LVEF %) (37.6 ± 13.3 vs 26.9 ± 9.2 , $p=0.003$) and lower estimated glomerular filtration rate (81.2 ± 22.5 vs 61 ± 34.3 ml/min/m², $p=0.03$). Arrhythmic death patients only had lower LVEF % than non-arrhythmic death patient's group.

Conclusions: In patients with ICD for secondary prevention QT, QTc, Tp-e duration and Tp-e index were not related to mortality.

Keywords: Cardioverter defibrillator; T peak-T end; ventricular arrhythmia

INTRODUCTION

Implantable cardioverter defibrillators (ICD) are the cornerstone therapy for preventing sudden cardiac death due to ventricular arrhythmias (1-3). Recent guidelines recommended ICD implantation with high level of evidence for secondary prevention of sudden cardiac death without reversible causes (4,5). Approximately 25% of the ICD implantations are for secondary prevention (6). Although there is no doubt about the utility of ICD in secondary prevention, the death from cardiac causes still occurred in this patients (1-3,7). Five years life expectancy of patients with ICD is between 62-64% (8). Therefore predicting and preventing mortality is important for patients with ICD.

T peak – T end (Tp-e) is the duration from the peak to end of t wave and reflects the distribution of electrocardiographic transmural repolarization (9). Tp-e is closely related with cardiac repolarization than total QT interval and any prolongation of Tp-e is related with malign ventricular arrhythmias (10,11). Additionally, it is known that Tp-e predicts sudden cardiac death even in patients with normal corrected QT (QTc) duration (12).

In this study we aimed to assess electrocardiographic ventricular repolarization parameters of patients with ICD for secondary prevention for predicting the mortality.

MATERIALS and METHODS

Study Population

Eighty-eight patients with ICD implantation for secondary prevention between January 2010 and January 2019 were enrolled to the study at Karadeniz Technical University hospital. Secondary prevention was defined as ICD implantation following ventricular tachycardia, ventricular fibrillation, and sudden cardiac death. Thirteen patients were excluded due to the absence of electrocardiographic, clinical and follow-up data. One patient with lead extraction, one patient with VT due to hypertrophic cardiomyopathy, two patients with Brugada syndrome and two patients with CRT implantation were also excluded. Coronary artery disease was defined as a history of more than 50% stenosis in any coronary artery, previous myocardial infarction, percutaneous coronary intervention, and coronary by-pass surgery. Ischemic cardiomyopathy was defined as myocardial dysfunction

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(left ventricular ejection fraction less than 50%) due to more than 50% coronary artery stenosis.

ICD indications for secondary prevention were accepted as documented sustained VT, VF, or sudden cardiac arrest (13). Patients were implanted single or dual chamber ICDs. Shock episodes and mortality data were obtained from hospital records. This study was approved by ethics committee of the Karadeniz Technical University.

Electrocardiographic Evaluation

For electrocardiographic evaluation previously obtained 12 derivation ECGs were analysed electronically (Mortara, ELI250c, USA, sheet speed 25 mm/s). Heart rate, QT and QTc intervals recorded. Tp-e was measured from precordial derivations by tail method. According to tail method; time interval between peak of the T wave and the point where T wave meets isoelectric line was measured (10). Tp-e interval was measured by two independent cardiologists and average of three consecutive beats was recorded. If interobserver difference was more than 20 ms, another measurement was obtained by a third cardiologist. Four patients excluded from the study due to discrepancy between all measurements. Tp-e tail index was defined as the ratio of Tp-e to QTc.

Statistical Analysis

Statistical analyses were performed by using the SPSS software (Version 23.0, SPSS, Inc., Chicago, IL). Variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they were normally distributed. Descriptive analyses were presented using medians and interquartile range (IQR) for non-normally distributed variables. Since age, left ventricular ejection fraction (EF), heart rate, QRS duration and QT-QTc values were normally distributed; independent sample T test was used to compare the differences in these parameters. Rest of continuous variables were non-normally distributed, Wilcoxon test was used to compare the differences. Chi-square test was used to compare categorical variables between presence of ICD shock and mortality groups. P-values less than 0.05 were considered statistically significant.

RESULTS

Mean age of the study population was 70.6±11.9 years. The study population was predominantly male [n = 53 (81.5%)]. Baseline demographic data of the patients are given in Table 1. Baseline demographic characteristics were similar between the mortality group. Indications for the secondary prevention ICD implantations of the 65 patients were; sustained VT in 48 (78.3%), VF in 11 (16.9%), sudden cardiac death (SCD) in 6 (9.3%). The majority of study patients [87.6% (n = 57)] were ischemic cardiomyopathy. However, ischemic etiology revealed no significantly difference between the groups on mortality (p= 0.16). Medications for heart failure and coronary artery disease rates were similar between two groups. Use of beta blocker (93.8 vs 81.3%, p = 0.13 respectively) and

amiodarone (78.1 vs 74.2%, p = 0.71 respectively), which may affect ECG parameters, were similar in both groups. The mean follow-up period was 54.3 ± 35.2 (4-145) months. During follow up, 17 (26.1%) of patients died. Patients who died were older (76.8±10.3 vs 68.7±12.5 years, p=0.009 respectively), had lower left ventricular EF % (26.9±9.2 vs 37.6±13.3, p=0.003 respectively) and lower eGFR values (61±34.3 vs 81.2±22.5 ml/min/m², p=0.03 respectively). 58 of the 65 patients (89.2%) had VVI ICDs. Having single or dual chamber ICD were similar about mortality rate (p=0.75 and 0.3, respectively).

Table 1. Baseline clinical characteristics, echocardiographic and laboratory findings of the study population

Variables	Alive (n=48)	Death (n=17)	p value	
Age (years)	68.7±12.5	76.8±10.3	0.009	
Male gender, n (%)	38 (79.2)	15 (88.2)	0.4	
HT, n (%)	33 (70.2)	13 (76.5)	0.62	
DM, n (%)	8 (16.7)	1 (5.9)	0.27	
CAD, n (%)	42 (87.5)	15 (88.2)	0.9	
Permenant AF, n (%)	14 (29.2)	8 (47.1)	0.18	
ACE inh., n (%)	34 (70.8)	13 (76.5)	0.65	
Beta blocker, n (%)	43 (89.6)	13 (76.5)	0.38	
MRA, n (%)	21 (44.7)	9 (52.9)	0.55	
ASA, n (%)	35 (72.9)	15 (88.2)	0.19	
P2Y12 inh., n (%)	18 (37.5)	5 (29.4)	0.54	
OAC, n (%)	14 (29.2)	8 (47.1)	0.18	
Statin, n (%)	38 (79.2)	13 (76.5)	0.81	
Amiodarone, n (%)	39 (81.3)	9 (60)	0.09	
LVEF (%)	37.6±13.3	26.9±9.2	0.003	
eGFR, ml/min/m ²	81.2±22.5	61±34.3	0.03	
Defibrillator type	Single chamber	44 (91.6)	14 (82.4)	0.3
	Dual chamber	4 (8.4)	3 (17.6)	

ICD: Implantable Cardioverter Defibrillator, HT: Hypertension, DM: Diabetes Mellitus, CAD: Coronary Artery Disease, AF: Atrial Fibrillation, ACE: Angiotensin Converting Enzyme, MRA: Mineral Receptor Antagonist, ASA: Acetylsalicylic Acid, OAC: Oral Anticoagulants, LVEF: Left Ventricular Ejection Fraction, eGFR: Estimated Glomerul Filtration Rate

The mean Tp-e and Tp-e index of all patients were 98.3±22 (56-170) ms and 0.22±0.04 (0.12-0.35), respectively. Heart rate, QRS, QT, QTc durations, Tp-e and Tp-e index values were similar among mortality groups (Table 2). Of the 17 patients with mortality, 3 died due to arrhythmia; two patients had VT and one had sudden cardiac death. Rest of deaths were deterioration heart failure (n=6), pneumonia and respiratory failure (n=3), multiorgan dysfunction (n=3), bronchial cancer (n=1) and myocardial infarction (n=1). When arrhythmic and non- arrhythmic deaths compared no significant difference obtained with heart rate, QT, QTc, Tp-e and Tp-e index except LVEF % (20 vs 30, p=0.021) (Table 3).

Table 2. Electrocardiographic variables among mortality patients

Variables	Alive (n=48)	Death (n=17)	p value
Heart rate, bpm	67.8±12.9	75.2±25.5	0.12
QRS duration, msec	131.5±33.9	170.9±62.3	0.1
QT, msec	427±60.4	431.7±61.8	0.78
QTc, msec	440±45.4	461.5±51.1	0.1
Tp-e, msec	100 (81-120)	96 (87-110)	0.77
Tp-e index	0.23(0.19-0.26)	0.21 (0.18-.024)	0.24

Continuous variables shown mean±SD and median (inter quartile range)

Table 3. Electrocardiographic variables among arrhythmic and non-arrhythmic deaths

Variables	Arrhythmic death (n=3)	Non-arrhythmic death (n=14)	P value
Age, years	86 (78-86)	74 (69-83)	0.19
Heart rate, bpm	71 (60-71)	66 (58-87)	0.3
QRS duration, msec	118 (115-118)	139 (114-159)	0.95
QT, msec	413 (401-413)	432 (364-501)	0.95
QTc, msec	442 (436-442)	461 (418-511)	0.77
Tp-e, msec	100 (81-120)	93 (83-110)	0.59
Tp-e index	0.23(0.19-0.26)	0.21 (0.17-.024)	0.36
LVEF (%)	20 (15-20)	30 (24-30)	0.021

Continuous variables shown median (inter quartile range)

DISCUSSION

ICD implantation is crucial for secondary prevention of sudden cardiac death, VF and VT (1-3,7). However, 5-years life expectancy in this patient group still remains at about 60% (9). In our study mortality was observed in 17 (26.1%) patients during the mean follow-up period of 4.5 years. Despite ICD therapy, SCD is still observed in this patient group. Direct or post-shock electromechanical dissociation, unsuccessful VT/VF therapy and refractory VT/VF were the explanation of SCD (10). It was also known that the majority of these patients die from respiratory failure or non-cardiac causes such as infectious diseases (11). Similar to the literature the majority of our study population deaths were non cardiac causes.

Tp-e, reflecting spatial distribution of ventricular repolarization (12), independently predicted both ventricular tachyarrhythmia and overall mortality in patients with low EF ($\leq 35\%$) and ICD (14). Every 10 ms increase in Tp-e value increased the risk of ventricular tachyarrhythmia by 14%. Despite the superior predictive value of Tp-e over QT and QTc for predicting sudden cardiac death in patients with heart failure, our study showed that Tp-e did not predict all cause and arrhythmic mortality in patients with ICD for secondary prevention. One of the explanation of our contradicted results

could be explained our study population properties. The majority of our study patients (90.7%) had a history of VT and lower EF which suggested the presence of ventricular scar. In the literature, the majority of patients were primary prevention. Additionally secondary prevention patients were not analysed as a subgroup.

Ventricular arrhythmias in the cardiomyopathy patients mostly originated ventricular scar tissue (11). Lower EF related denser scar in ventricle. This could potentially facilitate the presence of ventricular arrhythmias and effect ventricular repolarization and Tp-e values. Nevertheless cardiac magnetic resonance trial was shown there was no association between the repolarization parameters (QTc, Tp-e) and percent of LV scar or the amount of transmural scar (15). It is understood from here that the important thing is the presence of the scar, not its density or location. In our study Tp-e values were found to be similar between all cause and arrhythmic death group. Differentiation of Tp-e value may be only related to the presence or absence of scar.

LIMITATIONS

The most important limitation of this study was the small number of patients and the retrospective design. Some of the ECGs were obtained after ICD implantation. It should be considered that parameters such as QT, QTc and Tp-e which may predict ventricular arrhythmias could vary with time. However, it is a fact that risk classification of these patients can be done at any time. In our patient group, factors that could affect these parameters at the time of ECG such as the use of antiarrhythmic drugs and basal demographic characteristics were clearly demonstrated. We did not evaluate ventricular scar presence and/or density with cardiac MRI because of the retrospective design of study.

CONCLUSION

Tp-e, which indicates the distribution of electrocardiographic repolarization, are not predictive parameters for all cause and arrhythmogenic mortality in patients with secondary prevention ICD.

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