QT Dispersion Significantly Increases after Implantable Cardioverter-Defibrillator Shocks

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Objective: To determine whether QT dispersion (QTd), a noninvasive electrocardiographic parameter of ventricular tachyarrhythmia risk assessment, is changed by implantable cardioverter-defibrillator (ICD) shocks delivered during implantation process, to analyze the duration of these changes, and to further evaluate the effect of amiodarone on these parameters.

Methods: Twenty-six consecutive patients who are scheduled to undergo ICD implantation for aborted sudden cardiac death or documented symptomatic sustained ventricular tachycardia were enrolled into the study. A simultaneous 12-lead electrocardiogram (ECG) was recorded after the ICD implantation just before starting the testing shock when the patients were under general anesthesia (baseline record) and at 1st, 5th, 10th, 15th, 20th, 25th, and 30th minutes after the successful shocks. RR interval, QT interval, corrected QT interval (QTc), QTd, and corrected QTd (QTcd) were all measured and calculated on ECG.

Results: At 1st minute after the successful shock, an abrupt increase (from 67.0 ± 13.8 ms to 94.8 ± 21 ms, $P < 0.0001$) was observed in QTcd, which was followed by a gradual return to the preshock values at 20th minute. Analysis of patients with and without long-term oral amiodarone treatment showed that in amiodarone-pretreated patients QTcd returned to the baseline value earlier than in patients without amiodarone treatment (15 minutes vs 20 minutes, respectively).

Conclusions: ICD shocks cause an increase in QTcd lasting for up to 20th minute, which may predominate in some important clinical problems like electrical storm. Amiodarone, with the desirable effect on QTcd, may reduce the proarrhythmic effects of ICD shocks. **A.N.E. 2007;12(1):44-49**

implantable cardioverter-defibrillators; QT dispersion; electrical storm; amiodarone

Implantable cardioverter-defibrillators (ICDs) have begun to be used in primary and secondary prophylaxis of ventricular arrhythmias in an increasing number.^{1,2} Approximately 50 to 70% of patients treated with ICD receive appropriate device-based therapy within the first 2 years. However, electrical shocks delivered by ICD may have proarrhythmic effects as well, which may manifest as degeneration of monomorphic ventricular tachycardia into ventricular fibrillation, and the occurrence of "arrhythmic storms" after ICD implantation.^{3,4} "Arrhythmic or electrical storm" is defined as recurrent ventricular tachycardia or fibrillation occurring 2 or more times in a 24-hours period and requiring electrical cardioversion or defibrillation.^{5,6} Published data

suggest an overall incidence of arrhythmic storm approximately 10 to 30%.^{7,8} There are concerns about the occurrence of arrhythmic storm after ICD shocks^{3,4}; however, the exact mechanism of proarrhythmic effects of ICD shocks that may result in arrhythmic storm are currently poorly understood. Since shock-induced dispersion of ventricular repolarization caused by an electrical field stimulus has been suggested as a mechanism of ventricular fibrillation induction, the effects of electrical shocks on dispersion of ventricular repolarization were examined both experimentally,⁹ and clinically.¹⁰ In a previous study, Gurevitz et al.¹⁰ demonstrated that ICD shocks cause significant increase in the dispersion of myocardial repolarization as reflected by

QT dispersion (QTd) on the standard 12-lead electrocardiogram (ECG).

This study was sought to determine whether QTd, a predictor of increased risk for ventricular arrhythmias in patients with various cardiovascular diseases,^{11–16} is changed by transvenous endocardial ICD shocks delivered during implantation process and to analyze the duration of these changes.

MATERIALS AND METHODS

Twenty-nine consecutive patients who are scheduled to undergo ICD implantation for aborted sudden cardiac death or documented symptomatic sustained ventricular tachycardia were included in the study. Patients in whom the QT interval could not be measured in ≥ 3 leads or patients with the baseline rhythm of atrial fibrillation were excluded from the study. Pacemaker-dependent patients were also excluded. Finally 26 patients (18 men, 8 women, mean age of 56 ± 11) were found to be eligible for analysis. In each patient a multifunctional 3rd or 4th generation ICD device was implanted at morning hours. While single transvenous lead was used in 16 patients (Medtronic 7232 Cx [Medtronic Inc., Minneapolis, MN] in 5 patients, Guidant prizm 1860 [Guidant Corp., St. Paul, MN] in 5 patients, and Biotronik lexos VR [Biotronik GmbH&Co., Berlin, Germany] in 6 patients) dual transvenous leads were preferred in 10 patients (Biotronik lexos DR in 2 patients, Medtronic 7278 maximo in 3 patients, and Guidant prizm 1861 in 5 patients). Each patient had 1 biphasic test shock of 0.4 to 1.2 J (median 0.7 J) synchronized to the R wave during sinus rhythm, followed by 1 induction of ventricular fibrillation by T wave shocks or rapid burst ventricular pacing. Episodes of ventricular fibrillation were terminated by the device with a 5- to 31-J biphasic shock. The median energy of the shocks was 21 J. A simultaneous 12-lead electrocardiogram was recorded after the ICD implantation just before starting the testing shock when the patients were under general anesthesia (baseline record) and at 1st, 5th, 10th, 15th, 20th, 25th, and 30th minutes after the successful shocks. All ECGs were recorded at 75 mm/s paper speed with the EP Works-Mate (EP MedSystems, Inc., West Berlin, Germany) analogical polygraph system on which the same examiner measured QT and RR intervals digitally using cursor-moved calipers, and were analyzed by the same examiner blinded to the time of records.

QT interval was measured from the onset of the QRS deflection to the end of the T wave. Terminal portion of the T wave is defined as the intersection of the isoelectric baseline and the tangent of the maximal downward T wave slope. If a U wave was present the termination of the T wave was defined as the nadir between the T and U waves. If the U wave could not be discriminated from the T wave, QT interval was measured to the end of the U wave. The intraindividual variability between 2 separate measurements was $4.4 \pm 2.8\%$. Bazett's formula (Corrected QT (QTc) = $QT/\sqrt{RR}$) was used to correct the QT interval to the heart rate and QTc dispersion (QTcd) was calculated as the difference between the longest (max) and shortest (min) QTc intervals (QTcd = QTc max - QTc min).¹⁷

STATISTICAL ANALYSIS

The Statistical Package for the Social Science (SPSS for Windows 10.0 Chicago, IL, USA) was used for statistical analysis. Measures are reported as mean $\pm$ SD. Wilcoxon tests were used to evaluate the difference from baseline for each shock episode. A P value of <0.05 was taken as statistically significant.

RESULTS

Data from 26 patients (18 men, 8 women, with the mean age 56 ± 11 , ranging from 35 to 74 years) were used for final analysis. Clinical characteristics of the patients are listed in Table 1. Underlying cardiac disease was ischemic cardiomyopathy in 18 patients, idiopathic dilated cardiomyopathy in 6 patients, arrhythmogenic right ventricular dysplasia in 1 patient, and left ventricular noncompaction cardiomyopathy in 1 patient. Mean echocardiographic left ventricular ejection fraction was $34.8 \pm 8.9\%$ (range 25% to 55%) and left ventricular end-diastolic diameter was 5.9 ± 0.5 cm (range 4.6 cm to 6.4 cm). Changes in electrocardiographic parameters including RR interval, QTc max, absolute value of QTd, and QTcd at each time point are showed in Table 2. In total group of patients baseline mean QTcd was calculated as 67.0 ± 13.8 ms. Mean QTcd value after the shock was calculated as 94.8 ± 21.0 ms at the 1st minute, 89.8 ± 20.8 ms at the 5th minute, 82.3 ± 16.8 ms at the 10th minute, 73.7 ± 14.5 ms at the 15th minute 66.3 ± 12.7 ms at the 20th minute 66.4 ± 12.8 ms at the 25th minute, and 64.4 ± 12.3 ms at the 30th minute. QTcd at the 1st (P<0.0001), 5th (P<0.0001), 10th

Table 1. Clinical Characteristics of Patients

Characteristics	
Age (y)	56 ± 11(range: 35-74)
Sex	
Male (%)	18 (69%)
Female (%)	8 (30%)
Underlying heart disease	
Coronary artery disease	18
Idiopathic dilated cardiomyopathy	6
Arrhythmogenic right ventricular dysplasia	1
Noncompaction cardiomyopathy	1
Left ventricular ejection fraction (%)	34.8 ± 8.9 (range: 25-55)
Left ventricular end-diastolic diameter (cm)	5.9 ± 0.5 (range: 4.6-6.4)
Concomitant drug therapy	
Beta-blocker	18 (69%)
Digoxin	16 (62%)
Amiodarone	14 (53%)
Diuretics	20 (77%)
ACEi-ARB	22 (85%)
Spironolactone	12 (46%)

ACEi: Angiotensin converting enzyme inhibitors; ARB: Angiotensin II receptor blockers.

($P < 0.0001$), and 15th ($P < 0.01$) minutes after shock were found to be significantly higher than the baseline QTcd value. However QTcd at the 20th, 25th, and 30th minutes showed no statistically significant difference compared to the baseline value (Table 2 and Fig. 1). Analysis of patients with ($n = 14$, 58%) and without ($n = 12$, 42%) long-term oral amiodarone treatment showed that in amiodarone-pretreated patients (Table 2 and Fig. 2) QTcd returned to the baseline value earlier than in patients without amiodarone treatment (Table 2 and Fig. 3). According to these results after a maximum level ascertained at the 1st minute, QTcd began to decrease to its baseline value, which was achieved at the 20th minute in total study group and amiodarone-free group, and at the 15th minute in amiodarone-pretreated group. After these points no significant change occurred in QTcd. RR interval showed a significant but transient prolongation at the 1st minute after the shock in total patient population and in patients with amiodarone pretreatment. After shock QTc max also showed a significant prolongation that lasted for up to 15 minutes in total patient population, 10 minutes in amiodarone-pretreated patients, and 25 minutes in patients without amiodarone pretreatment. Persistence of postshock increments in absolute value of QTd is 20 minutes in total patient population, 15 minutes in amiodarone pretreated patients, and 20 minutes in patients without amiodarone pretreatment.

Comparison between male ($n = 18$) and female ($n = 8$) patients demonstrated no significant difference in observed dynamics.

DISCUSSION

This study showed that in humans ICD shocks cause significant increase in OT dispersion which lasts for 20 minutes after the shock delivery. These findings are consistent with previous animal and clinical studies and may be accepted as one of the underlying mechanisms of shock-induced proarrhythmia. Although Gurevitz et al.¹⁰ reported an increase in QTd after ICD shocks for the first time in humans, the question of how long this effect continues was analyzed systematically in our study. We also examined the effect of long term amiodarone use on postshock QTd increase and demonstrated an earlier return to the baseline in this patient population.

In a previous report Boriani et al.¹⁸ showed a significant increase in QTd after successful internal atrial cardioversion for atrial fibrillation. Since they reported no increase in QTd after unsuccessful shocks, they could not explain the increase in QTd is because of either the direct effect of shock or conversion to sinus rhythm. In our study, the baseline rhythm of sinus was established after termination of ventricular fibrillation episode in each patient. Therefore the prolongation of QTd should

Table 2. Comparison of Observed Dynamics with Basal Values in Total Patient Population, and in Patients with and without Amiodarone Pretreatment

	Basal	1st minute	5th minute	10th minute	15th minute	20th minute	25th minute	30th minute
Total patient population (n = 12)								
RR interval	832.2 ± 91.0	885.5 ± 103.9*	861.3 ± 91.1	857.3 ± 88.7	860.3 ± 82.6	845.9 ± 74.7	847.0 ± 70.0	851.5 ± 82.3
QTc max	541.4 ± 56.1	580.0 ± 57.8†	582.05 ± 50.1†	562.9 ± 47.9‡	546.3 ± 49.2	547.5 ± 42.9	546.6 ± 44.7	534.5 ± 45.6
QTd	61.1 ± 13.3	92.9 ± 16.9†	83.2 ± 20.2†	76.3 ± 16.9†	68.3 ± 14.6*	60.7 ± 11.4	61.1 ± 11.9	59.3 ± 11.3
QTcd	67.0 ± 13.8	98.8 ± 15.9†	89.8 ± 20.8†	82.3 ± 16.8†	73.7 ± 14.5*	66.3 ± 12.7	66.4 ± 12.8	64.4 ± 12.3
Patients with amiodarone pretreatment (n = 14)								
RR interval	851.0 ± 89.0	931.7 ± 94.7‡	893.6 ± 83.3	895.0 ± 89.1	897.1 ± 75.2	878.5 ± 65.7	876.8 ± 66.0	882.9 ± 75.61
QTc max	552.2 ± 52.3	576.6 ± 63.4*	580.5 ± 49.3*	553.21 ± 38.6	530.3 ± 27.4	536.3 ± 37.7	537.8 ± 34.9	527.1 ± 32.9
QTd	65.4 ± 11.9	99.4 ± 16.0§	87.7 ± 21.0§	83.2 ± 16.7§	71.4 ± 15.3	65.3 ± 7.9	64.8 ± 9.7	61.3 ± 10.2
QTcd	71 ± 13.2	103.4 ± 16.4§	92.9 ± 21.1*	88.0 ± 16.9§	75.5 ± 15.5	70.0 ± 10.0	69.5 ± 11.0	65.7 ± 12.2
Patients without amiodarone pretreatment (n = 12)								
RR interval	809.0 ± 91.6	831.6 ± 89.8	823.6 ± 88.3	813.5 ± 67.8	817.2 ± 71.1	807.9 ± 68.3	812.2 ± 59.5	814.8 ± 77.0
QTc max	528.7 ± 59.8	584.0 ± 53.2*	583.0 ± 51.4*	574.3 ± 56.5*	565.0 ± 62.6*	560.4 ± 46.6*	550.0 ± 53.6	543.1 ± 57.3
QTd	56.0 ± 13.6	85.4 ± 15.4*	77.8 ± 18.6*	68.1 ± 13.7*	64.6 ± 13.3*	55.4 ± 12.1	56.6 ± 13.1	57.0 ± 12.6
QTcd	62.4 ± 13.5	93.5 ± 14.2*	86.1 ± 20.7*	75.7 ± 14.5*	71.7 ± 13.5*	61.9 ± 14.5	62.8 ± 14.2	62.9 ± 12.7

Data are reported as mean ± SD. All values are in ms.

*P < 0.01, †P < 0.0001, ‡P < 0.05, §P ≤ 0.001.

Figure 1. Changes in QTcd over time in total patient population. Significantly increased postshock QTcd has returned to the baseline value at 20th minute of successful shock.

be related to the shock itself rather than any other factor.

The mechanisms responsible for postshock increase in QTd are not clear. Since sympathetic stimulation was previously shown as a mechanism for increased dispersion of myocardial repolarization, systemic and myocardial sympathetic stimulation caused by electrical shocks might be a reason for increased QTd.^{19–21} In addition to this it was experimentally demonstrated that epicardially applied electrical shocks cause significant changes in effective refractory period only in areas apical to the electrodes, which result in inhomogeneous refractoriness.²² "Electroporation" defined as the microscopic breaks in the cardiomyocyte membrane around the shock-delivering catheter is another suggested mechanism for the explanation

Figure 2. QTcd showed a more rapid decline to the baseline value (at 15th minute) in amiodarone-pretreated patients.

Figure 3. In patients without amiodarone treatment, QTcd showed a similar course to total patient population.

of postshock increased dispersion of repolarization via prolonged refractory period only in the affected area.^{23,24} Ventricular arrhythmias preceding the shock are another possible explanation for the dispersion of myocardial repolarization via ischemia.¹⁹

The proarrhythmic effects of ICD shocks may have a role in the etiology of electrical storm³ and the increase in QTd lasting for up to 20 minutes (15 minutes in amiodarone pretreated patients) after shock may be partially responsible for the recurrence of arrhythmia. In a study by Credner et al.,³ the incidence of electrical storm was reported as 10% and amiodarone, an agent that decreases the QTd,²⁵ was found to be effective for the treatment of these storms. In our study amiodarone led to the earlier establishment of baseline QTd values. In the light of this finding we suggest that avoidance of long lasting dispersion of repolarization with use of amiodarone might be an explanation for the effectiveness of amiodarone in the treatment of electrical storm. In patients with ICD, amiodarone should be preferred to the other agents, which increase QTd.

Since gender differences in human electrocardiographic parameters and rate of sudden cardiac death exist,^{26,27} we compared all electrocardiographic parameters between male and female patients. Although previous studies showed that women have faster resting heart rate and longer QTc than do men, we could not demonstrate any difference probably because of the small number of patients. Larger studies are needed to evaluate the sex-related differences in ICD patients.

STUDY LIMITATIONS

This study was not designed to evaluate the relation between shock energy or arrhythmia duration with QT dispersion. Small sample size along with relatively wide ECG analysis intervals (5 minutes) after shocks is the most important limitation of the study. Lack of comparability between amiodarone-free and amiodarone-pretreated patients regarding all parameters is another limitation.

In conclusion, ICD shocks cause an increase in QTcd up to 20 minutes, which may predominate in some important clinical problems like electrical storm. Amiodarone, with the desirable effect on QTd, may reduce the proarrhythmic effects of ICD shocks.

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