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Exploring QT interval changes as a precursor to the onset of ventricular fibrillation/tachycardia☆

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Abstract In the present study, we have retrospectively analyzed the corrected QT (QTc) interval before spontaneous episodes of sudden cardiac arrest in patients with a wearable cardioverter defibrillator. Corrected QT interval was measured for all normal beats from 32 recordings of baseline rhythm and compared to normal rhythm before a paired spontaneous cardiac arrhythmia. Before arrhythmia, the QTc (505 ± 73 ms) was not significantly longer than the baseline rhythm (497 ± 73 ms) (P = .23). Considering ventricular tachycardia (VT) events only (12 patients), event QTc (526 ± 75 ms) was not significantly longer than baseline QTc (520 ± 74 ms) (P = .41). Considering fast VT/ventricular fibrillation (VF) events only (20 patients), event QTc (494 ± 70 ms) was not significantly longer than baseline QTc (483 ± 71 ms) (P = .26). The influence of QTc as a measure to indicate an impending VT event in a variety of VT/VF patients remains unclear.

Keywords: QTc interval; Ventricular tachycardia; Ventricular fibrillation; Sudden cardiac arrest; Arrhythmia

Introduction

Sudden cardiac arrest (SCA) is the leading cause of death in the United States claiming approximately 450 000 lives per year, more than stroke, lung cancer, breast cancer, and AIDS combined.[1-4] Sudden cardiac arrest is caused by arrhythmias or abnormal rhythms of the heart muscle and occurs most often in patients with clinically recognized heart disease including myocardial infarction and heart failure. However, there is only an estimated 5% out-of-hospital survival rate in the United States for SCA due to the inability to treat the SCA event within a short period.[5-7] Because SCA events are mostly unwitnessed and difficult to treat in time, therapies are needed to prevent the event to increase survival. Implantable cardioverter defibrillators (ICDs) and wearable cardioverter defibrillators (WCDs) are 2 types of therapies for prevention of sudden cardiac death after SCA has occurred. Only a small number of patients qualify for ICD therapy, and such therapy is expensive with implantation costs up to $50000.[8] The WCD therapy helps treat patients who require short-term to long-term care with less cost than an ICD. However, both therapies are less costly than hospitalization that costs up to $3000/d.[9] The ZOLL Lifecor LifeVest (Pittsburgh, PA) WCD (Fig. 1), the first wearable defibrillator that offers immediate shock therapy to unresponsive patients having a ventricular tachycardia (VT) or ventricular fibrillation (VF), is the foundation of this study.

There has been a considerable amount of work to investigate the mechanism behind the onset of spontaneous ventricular arrhythmias, VT and VF, by comparing measures between a patient's normal sinus rhythm and onset to arrhythmia recordings in hopes of preventing such cardiac events.[10-12] The results have indicated that measures that predict the onset of spontaneous VT/VF events include an increase in heart rate (HR), changes in HR variability, T-wave alternans, the type of onset including premature ventricular contractions (PVCs), and the increased rate corrected QT (QTc) interval where changes have been observed before an arrhythmia.[13-18]

Shortening of the QT interval before the onset of ventricular arrhythmias has been seen in patients without

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Fig. 1. ZOLL Lifecor LifeVest.

structural heart disease.[19] A similar study further investigated the length of the QT interval in patients with structural heart disease via electrocardiograms (ECGs) stored within the ICD. A prolonged QTc interval, using Bazett's formula, was found before the onset of ventricular arrhythmias (onset QTc, 518 ± 67 ms; baseline QTc, 450 ± 61 ms).[20] Whether similar changes can be seen within the orthogonal ECGs of a diverse group of WCD patients who have ventricular arrhythmia has yet to be established.

The present retrospective study compares in patients with a WCD the duration of the QTc interval before spontaneous VT/VF events with the QTc interval from the baseline ECG recording.

Methodology

Data

Electrocardiograms recorded by the WCD device were analyzed in this study. The wearable cardioverter defibrillator is worn outside the body and continuously monitors the heart via dry, nonadhesive sensing electrodes and is able to deliver a shock to the patient with separate therapy electrodes. The wearable cardioverter defibrillator records 2 orthogonal ECG leads at a sampling rate of 100 Hz—a side-to-side data channel and an anterior/posterior data channel. The side-to-side ECG channel was used for this analysis. Each patient included in the analysis had a normal sinus rhythm recording at baseline, to determine the normal QRS morphology, and a VT or ventricular fibrillation arrhythmia episode recording. To calculate the corrected QT interval, only patients who had a normal rhythm before arrhythmia onset during the event episode were included in this analysis (refer to Fig. 2 for a representative patient's baseline rhythm and rhythm before onset of an arrhythmia episode). Fast VT and VF events demonstrated erratic disorganized behavior greater than 250 beats per minute (bpm), and VT events were ventricular arrhythmias between 150 and 250 bpm.

The 32 patients analyzed for the study had an average recording length before event of 14 seconds (range, 5-18 seconds) and an average baseline recording length of 52 seconds (range, 34-124 seconds). Time lapse between baseline and arrhythmia recordings was 4 ± 12 months. Of the 32 patients, there were 20 patients with fast VT/VF (>250 bpm) and 12 patients with VT. Thirty-one patients had demographic information available. The average age was 62 years, and 71% of the patients were male. The primary diagnoses leading to the prescription of the WCD were recent myocardial infarction, ICD removal due to infection, and sudden cardiac arrest with ICD implantation delayed (see Table 1 for all clinical details).

QT and RR measurement

An automated computer program was developed using Matlab (Mathworks, Natick, MA) to process the WCD ECG signal and to locate the characteristic points typical of a normal ECG including the Q wave, R wave, and the end of the T wave. Because the dataset was relatively small and to ensure that all automated measurements were accurate, the data were manually overread and corrected as necessary. All ectopic beats were discarded from the analysis (refer to Fig. 3 for example recordings of an ectopic beat in both the normal

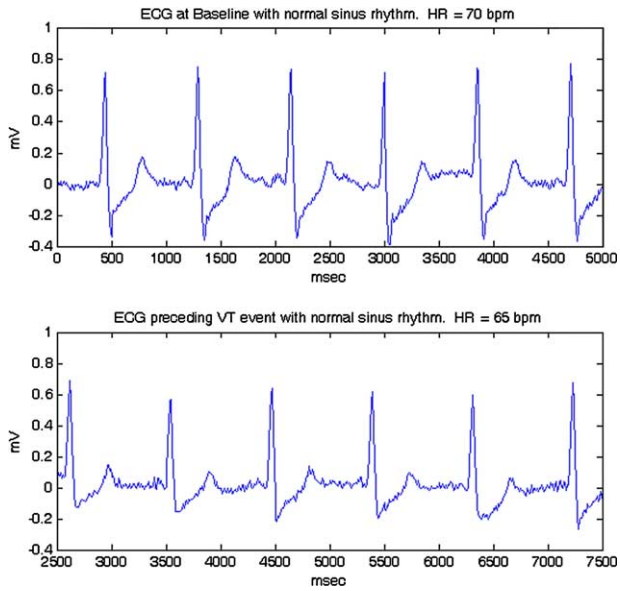

Fig. 2. Upper panel, baseline ECG with normal sinus rhythm. Lower panel, five seconds of ECG preceding a VT event.

Table 1
Clinical characteristics

	All[a] (%)	VF[a] (%)	VT (%)
No. of patients	n = 32	n = 20[a]	n = 12
Age (y) (mean ± SD)	62 ± 10	60 ± 11	63 ± 11
Males	22 (71)	14 (74)	8 (67)
Diagnosis			
Myocardial infarction	9 (28)	6 (30)	3 (25)
ICD pocket infection	8 (25)	4 (20)	4 (33)
Cardiac arrest/waiting for ICD	8 (28)	4 (20)	4 (33)
Other	7 (22)	6 (30)	1 (9)
Onset characteristics			
Sudden	6 (19)	3 (15)	3 (25)
PVC/SLS	26 (81)	17 (85)	9 (75)

SLS indicates short-long-short.
[a] One patient was without demographic information.

sinus rhythm and before the event for a single patient). Once the relative locations of these fiducial points were found, both the QT and RR intervals were calculated.

A corrected QT interval was measured using linear scaling method proposed by Rautaharju and Zhang.[21] This correction method reduces the heart rate–dependent distortion that is present in other methods such as Bazett's. Equation (1) describes the adjustment used where RR is the distance between R wave to R wave in seconds, QT is the distance between the Q wave and T wave in seconds, and the scaling factor is dependent on the sex of the patient.

Equation 1: Corrected QT interval

$$\begin{aligned}\text{Males}: QTc &= QT + 0.360*(1 - RR^{0.5}) \\ \text{Females}: QTc &= QT + 0.353*(1 - RR^{0.5})\end{aligned}. \quad (1)$$

The rate of the arrhythmia was found and classified by a physician. The measurements were divided up into 2 groups based upon rate as follows: VT and fast VT/VF.

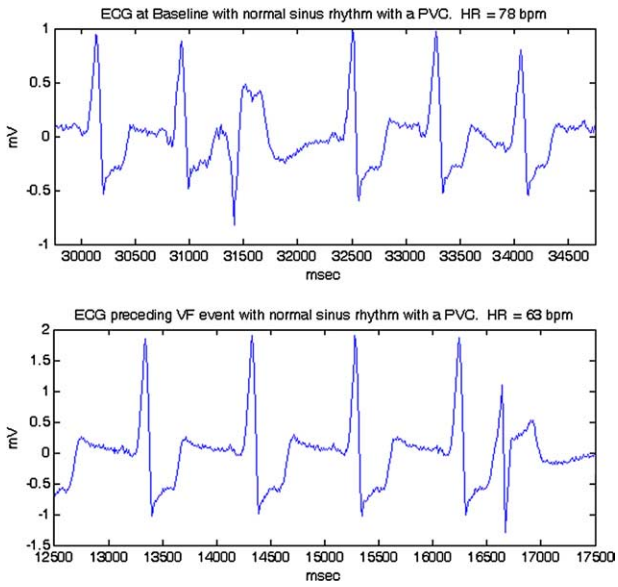

Fig. 3. Upper panel, baseline ECG with normal sinus rhythm with a premature ventricular complex. Lower panel, electrocardiogram preceding VF event with an early premature ventricular complex on top of the T wave.

Onset definition

In this case, we separate the study population into 2 groups as follows: sudden onset and nonsudden onset. The sudden onset group was defined by arrhythmias that were not preceded by a ventricular ectopic beat. The nonsudden group was defined by arrhythmias that were preceded by a PVC. This group includes arrhythmias preceded by a visible premature ventricular contraction or those arrhythmias that were preceded by a short-long-short sequence. The *short-long-short sequence* for this analysis was defined as a normal sinus beat followed by a premature ventricular contraction followed by a ventricular escape beat followed by a PVC initiating the arrhythmia.

Statistical analysis

The averaged QTc measurement and heart rates for both the normal sinus rhythm and onset to arrhythmia recordings were compared for each patient using Student paired *t* test. Differences with $P \leq .05$ were considered statistically significant. Results are expressed as mean ± SD.

Results

QTc before arrhythmia onset

Refer to Table 2 for all patients' averaged QTc and HR measures and for overall average QTc and HR by arrhythmia type. For all arrhythmias, the overall average QTc measurement was increased before the arrhythmia (505 ± 73 ms) but not significantly prolonged as compared to the baseline rhythm (497 ± 73 ms) ($P = .23$). The baseline QTc was more

Table 2
All patients and arrhythmia type (normal sinus rhythm vs before arrhythmia)

	Baseline	Onset	P[a]
All patients			
No. of patients	n = 32		
No. showing QTc increase	20 (63%)		
No. with baseline QTc >500 ms	18 (56%)		
No. showing HR increase	19 (59%)		
Arrhythmia rate (bpm) (mean ± SD)	251 ± 55		
QTc (ms) (mean ± SD)	497 ± 73	505 ± 73	.23
HR (bpm) (mean ± SD)	76 ± 16	85 ± 24	.029
Fast VT/VF			
No. of patients	n = 20		
No. showing QTc increase	11 (55%)		
No. with baseline QTc >500 ms	10 (50%)		
No. showing HR increase	10 (50%)		
Arrhythmia rate (bpm) (mean ± SD)	281 ± 46		
QTc (ms) (mean ± SD)	483 ± 71	494 ± 70	.26
HR (bpm) (mean ± SD)	80 ± 18	84 ± 19	.25
VT			
No. of patients	n = 12		
No. showing QTc increase	10 (83%)		
No. with baseline QTc >500 ms	8 (67%)		
No. showing HR increase	9 (75%)		
Arrhythmia rate (bpm) (mean ± SD)	200 ± 22		
QTc (ms) (mean ± SD)	520 ± 74	526 ± 75	.41
HR (bpm) (mean ± SD)	70 ± 12	87 ± 32	.026

[a] Baseline vs onset.

Table 3
Onset type (normal sinus rhythm vs before arrhythmia)

	Baseline	Onset	P[a]
Sudden onset			
No. of patients	n = 6		
No. showing QTc increase	4 (67%)		
No. with baseline QTc >500 ms	3 (50%)		
No. showing HR increase	4 (67%)		
Arrhythmia rate (bpm) (mean ± SD)	245 ± 71		
QTc (ms) (mean ± SD)	509 ± 118	489 ± 63	.35
HR (bpm) (mean ± SD)	81 ± 26	83 ± 15	.41
Nonsudden onset			
No. of patients	n = 26		
No. showing QTc increase	17 (65%)		
No. with baseline QTc >500 ms	15 (58%)		
No. showing HR increase	15 (58%)		
Arrhythmia rate (bpm) (mean ± SD)	252 ± 53		
Coupling interval (ms) (mean ± SD)	541 ± 226		
Prematurity index (ratio) (mean ± SD)	0.76 ± 0.41		
QTc (ms) (mean ± SD)	494 ± 62	509 ± 76	.14
HR (bpm) (mean ± SD)	75 ± 14	85 ± 26	.026

[a] Baseline vs onset.

than 500 milliseconds in 18 (56%) of the patients. Considering VT events only (12 patients), event QTc (526 ± 75 ms) was not significantly longer compared to baseline (520 ± 74 ms) (P = .41), and 8 (67%) of the patients had a baseline QTc more than 500 milliseconds. Considering fast VT and VF events only (20 patients), event QTc (494 ± 70 ms) was not significantly prolonged compared to baseline (483 ± 71 ms) (P = .26), and 10 (50%) of the patients had a baseline QTc more than 500 milliseconds.

Heart rate before arrhythmia onset

Refer to Table 2 for all patients' average HR measurements and for overall average HR by arrhythmia type. The overall average HR was found to be significantly increased before the arrhythmia (85 ± 24 bpm) when compared to baseline (76 ± 16 bpm) (P = .029). Considering VT events only (12 patients), event HR (87 ± 32 bpm) was significantly faster compared to baseline (70 ± 12 bpm) (P = .026). Considering fast VT and VF events only (20 patients), event HR (84 ± 19 bpm) was not significantly faster compared to baseline (80 ± 18 bpm) (P = .25). It appears that the overall HR difference is mostly attributed to the group that experienced a VT event rather than a fast VT/VF event given their respective P values (P = .026; P = .25).

Modes of arrhythmia onset

Table 3 contains all patients' QTc and HR measurements by arrhythmia onset type. Considering sudden onset events only (6 patients), event QTc (489 ± 63 ms) was not significantly prolonged compared to baseline (509 ± 118 ms) (P = .35), and event HR (83 ± 15 bpm) was also not significantly faster compared to baseline (81 ± 26 bpm) (P = .41). The baseline QTc was more than 500 milliseconds in 3 (50%) of the patients.

Considering nonsudden events only (26 patients), event QTc (509 ± 76 ms) was not significantly prolonged compared to baseline (494 ± 62 ms) (P = .14). Event HR (85 ± 26 bpm) was significantly higher compared to baseline (75 ± 14 bpm) (P = .026). The baseline QTc was more than 500 milliseconds in 15 (58%) of the patients.

Both ECG leads were used to determine the morphology of the PVC that initiated the arrhythmia in the nonsudden group. In 4 (15%) of the 26 patients, the premature ventricular contraction was initiated by a premature supraventricular ectopic stimulus. In the other 22 patients, the premature ventricular contraction was caused by a ventricular ectopic beat.

This finding suggests that the mode of onset could also play a role in the HR dynamics before onset as the nonsudden group demonstrated a significant increase in HR before event, whereas the sudden onset group did not (P = .026; P = .41).

Discussion

This retrospective study describes the changes in the QTc interval and heart rate before fast VT/VF and VT in patients with a WCD. After investigating various groups including arrhythmia type and onset, a significant change in QTc was not found, when comparing baseline to onset of a ventricular arrhythmia. A significant change was found in HR for the overall group, the PVC/short-long-short onset group, and the VT group.

Baseline QTc in our high-risk population was elevated. More than half (56%) of our patients had a baseline QTc greater than 500 milliseconds that limits the prospects that a further increase would occur before a VT. Although 63% did show an increase in QTc, it was not statistically significant due to the elevated baseline QTc.

Such findings cannot confirm or dispute results found by prior studies in which an elongated QTc precedes a spontaneous VT[20] or where the QT interval was shorter before a VT.[19] The methods for calculating QTc interval were different, and our study populations were very different.

Diem et al[20] analyzed 228 episodes of VT in 52 patients. They found the QTc interval (518 ± 67 ms) before the arrhythmia was statistically significantly prolonged as compared to baseline QTc (450 ± 61 ms). Baseline QTc (515 ± 86 ms) in our study was comparable to the event QTc found by Diem et al.[20]

Fei et al[19] compared the QT interval before VT to a baseline 40 minutes prior in 10 patients (aged 38 ± 16 years). They found the QT interval significantly shorter before the arrhythmia when compared to baseline (342 ± 34 ms vs 353 ± 35 ms; P < .001), but they did not correct for HR.[19]

The physiologic mechanism behind why some groups demonstrate a prolonged QTc before ventricular arrhythmia remains unclear. With larger populations and long-term records, interesting relationships may emerge. To further validate these results, more patients for each group are needed.

The nonsudden group may be more vulnerable to PVC-triggered arrhythmias if their QTc is also prolonged,

exposing them to greater risk of a depolarization occurring during the relative refractory period. Whether an arrhythmia is triggered by a PVC, a sequence of PVCs, or has a sudden onset has been studied by Leenhardt et al.[14] They confirmed the presence of PVCs within the 20 minutes before ventricular tachyarrhythmic episodes, more so in rapid episodes with rate of more than 160 bpm than in comparison to rates less than 160 bpm.

In many of the comparisons, HR was statistically significant when comparing baseline to sinus rhythm before arrhythmia onset. Although HR may be a very sensitive measure for various disease states, it is not very specific. There are many factors that influence HR including environment, exercise, and pharmacologic treatment. Thus, HR needs to be discussed in context rather than used as a stand-alone predictor.

Overall, our findings were limited to the number of patients with available normal ECG rhythm before the onset of an arrhythmia, and a quality baseline was required for a comparison to event data. Of the available patients, an overall limitation was the minimal recording length of the onset of an arrhythmia. If longer onset recordings were available for minutes or hours or days before the event rather than seconds, not only the parameters of interest could be further investigated but also other characteristics, such as HR variability, that could not be evaluated in the limited recordings may prove to be significant. Also, because the baseline recordings were not 24-hour recordings, we were unable to calculate HR and QTc with respect to circadian influences.

Further patient history is also needed to determine if the significant findings are an artifact of pharmacologic treatment (eg, β-blockers or QTc-prolonging antiarrhythmics) or truly exist. The information available to us was only that which was recorded for ordering purposes.

An important limitation of our analysis was the small sample size. As we begin to investigate other factors that may aid in stratifying the population, a larger sample size is required. With a larger population, we would be able to further stratify the arrhythmia type into monomorphic VT, polymorphic VT, and VF as their mechanisms are very different. For the case of sudden vs nonsudden onset, the distributions across the arrhythmia type were relatively consistent (75%-85% for nonsudden and 15%-25% for sudden onset). If an ECG marker can be determined to be a risk stratifier or predictor for an arrhythmia event, then a well-designed prospective study will need to be performed to evaluate the predictive power of such an index.

Should an ECG marker such as QTc prolongation prove to be sensitive to an impending arrhythmia, this information could benefit WCD patients by adapting detection algorithms to reduce false shocks or initiate a gentler therapy such as surface antitachycardial pacing. This impending arrhythmia marker would most likely also not be very specific in that there could be many instances where the marker appears but is not followed by a malignant event. Long-term recordings will help answer the risk of false alarms, and more sophisticated computational methods could be used to reduce this risk.

Conclusion

The influence of QTc as a measure to indicate an impending ventricular arrhythmia in a variety of VT/VF patients remains unclear because there was no statistical difference between the QTc in baseline and onset to arrhythmia recordings.

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