Effect of Body Position on the Measurements of Early and Late Cardiac Repolarization Duration

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Abstract

In this study, we assessed the impact of changes in body position on our novel parameters quantifying repolarization heterogeneity based on the morphology of the T-loop. Early and late repolarization durations (ERD and LRD) as well as QT/QTc, RR and T-wave amplitude were computed from the three pseudo-orthogonal lead (X, Y Z) recorded in healthy individuals. These measurements were monitor continuously in 63 individuals undergoing experiment including five body positions: left supine, right supine, supine, standing and sitting.

We observed more profound impact of body position changes onto the QT/QTc interval and heart rate than in TpTe, ERD and LRD intervals. We conclude that the ERD and LRD interval measurements are more robust to changes in autonomic balance and heart position triggered by body position shifts.

1. Introduction

Repolarization heterogeneity has been recognized as a crucial factor required for the triggering and maintaining of life-threatening ventricular arrhythmias [1]. Yet, there is a lack of valid markers quantifying an increase in repolarization heterogeneity from the surface ECGs. Inter-lead QT dispersion was used for years but it has been progressively abandoned because it is primarily driven by measurement artifact [2].

Because increased roundness of the T-loop is associated with increased heterogeneity, we developed early and late repolarization duration indices (ERD and LRD) to capture subtle changes of T-loop morphology [3]. The investigation of these novel indices led to an encouraging number of successful clinical results [3,4] such as: 1) improved detection of individuals exposed to subtle I_{kr}-blocking compounds (moxifloxacin [5] and sotalol [6]), 2) better discrimination of cardiac patients with a history of dangerous ventricular arrhythmias, and 3) independent prediction of syncope and appropriate ICD therapy in MADIT II type patients [7].

In order to understand better how these parameters are affected by heart rate and the autonomic regulation of the heart, we implemented an experiment during which continuous ECGs were acquired in healthy individuals undergoing body position changes. We analyzed the static and dynamic profiles of ventricular repolarization quantifiers under different body positions. Then, we discuss the impact of different autonomic regulation on different ECG measurements.

2. Methods

The design of this study was a longitudinal positional study. Each patient was placed in a series of positions for approximately two minutes each. During this time, Holter ECGs were continuously recorded while flagging the time when the body positions were changed. The experiment included: left supine, right supine, supine, standing, and then sitting positions.

2.1. Study population

This study involved ECG tracings from sixty-five healthy individuals that were enrolled at the University of Rochester Medical Center following approved protocol from the Investigational Review Board of the University of Rochester (NY). The population had an average age of 38±13 years ranging from nineteen to sixty-five years old. Forty-one of the sixty-five patients were females.

2.2. ECG recordings

The ECG was recorded using a pseudo-orthogonal lead configuration (X, Y and Z), the sampling frequency of the signal was 200 Hz and the amplitude of the signal was coded on 10 bits (Burdick, Inc.,Milton, WI).

2.3. Scalar ECG measurements

The RR and QT interval measurements were based on COMPAS, a software package developed at the University of Rochester Medical Center. Each measurement was calculated using eigenvectors from

applying principle component analysis (PCA) applied to leads X, Y, and Z. COMPAS provided the end of the T-wave by calculating the intersecting point between the baseline and the descending slope of the T-wave [8].

The T-wave apex was determined by fitting a parabola to the T-wave. The maximum of the parabola defined the location of the T-wave apex. TpTe was calculated from QT and QT apex such that TpTe = QT – QT apex. Baseline wander was corrected by the cubic spline interpolation method.

2.4. Vectocardiographic measurements

ERD and LRD are calculated from the T-loop when it is in its preferential plane, which is defined by two eigenvectors computed from PCA applied to leads X, Y, and Z.

Vmax is the maximum length of the repolarization heart vector (close on the scalar ECG to the time of the apex of the T-wave). The ERD is an interval along the T-loop path towards the QRS complex, whereas LRD is towards the end of the T-wave. Both are expressed in msec and are associated with a percentage representing the duration needed by the heart vector to travel from its maximum value to that percentage of Vmax. For example, $LRD_{30\%}$ represents the duration from Vmax to 30% of Vmax towards T-end. These intervals are prolonged when the repolarization process is delayed or/and when the T-loop roundness is increased.

2.5. Statistical analysis

We implemented analyses of the dynamic and static profiles of the investigated repolarization parameters. The interval defined for the static analysis was the last 30 seconds of each position. First, the median values were calculated for each patient then the population-based median and standard deviations were reported. The supine position was compared to standing and sitting for each parameter using a student's paired t-test.

When investigating the dynamic profile of the repolarization parameters, the population-based median of each parameter was taken over a 2 second interval for each patient. This median was then taken at each time point and plotted across time over 84 seconds. Time zero indicates the time at which the subjects switch to the reported body position.

3. Results

3.1. Measurements after repolarization adaptation to body changes (static period)

Sixty-one of the original sixty-five patients were included in table 1. The four ECGs not used were discarded because of technical issues during the recording.

Table 1 describes the changes (Δ) of RR, QT, QTcF (Fridericia rate correction), QTcB (Bazett rate correction) ERD, and LRD intervals for 30, 50 and 70%. The differences between supine and standing resulted in significantly higher values for RR and QT and significantly lower values for QTcB and $LRD_{70\%}$. Comparing between supine and sitting position revealed significant increases for RR, QT, QTcF, and TpTe as well. The RR values for sitting minus standing were found to be significantly different (80±73ms).

Table 1: Results from comparing the last 30 seconds of supine to the last 30 seconds of standing and sitting. A significant difference (*p<0.05, **p<0.001), median ±standard deviation are reported.

Δ (MS)	Supine-Stand (n=61)			Supine-Sitting (n=61)		
RR	120**	±	109	37**	±	75
QT	16.2**	±	14.9	12.4**	±	11.3
QTcF	-1.9	±	10.3	7.1**	±	8.5
QTcB	-43.3**	±	44.1	-3.9	±	28.9
TpTe	-0.04	±	12.32	1.28*	±	3.59
ERD30	-0.62	±	8.08	0.04	±	6.08
ERD50	-2.50	±	9.96	0.08	±	6.69
ERD70	-1.23	±	20.26	2.13	±	13.63
LRD30	-0.16	±	4.76	0.86	±	4.18
LRD50	-0.78	±	6.87	0.57	±	5.01
LRD70	-12.30*	±	37.35	-1.27	±	13.87

3.2. Measurements during repolarization adaptation triggered by body changes (dynamic profiles)

Ten of the sixty-one usable files had positions that lasted less than the 70 seconds. These files were discarded leaving fifty-one subjects in figures 1 and 2.

The beginning of the plots in figure 1 show a large decrease in RR that occurred as the patients stood from a supine position as well as an increase in the QTcF. Figure 1 also displays that RR is adapting throughout the entire 70 seconds of the plot.

Figure 2 shows decreases in the duration of TpTe and $ERD_{30\%}$ right at the beginning of standing. Both quickly leveled off approximately 5 seconds after the positional switch. $LRD_{30\%}$ did not follow this trend and stayed level throughout the positional change. However, $ERD_{50\%}$, $ERD_{70\%}$, $LRD_{50\%}$ and $LRD_{70\%}$ all displayed results similar to TpTe and $ERD_{30\%}$ (not shown).

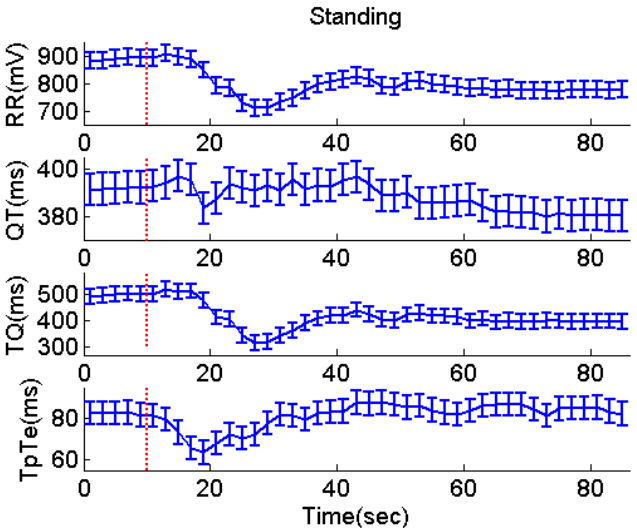

Figure 1: Plot of the median values of RR, QT, TQ and TpTe with a 90% CI over the 84 seconds. The postural change occurs at the dashed line at the 10 second mark.

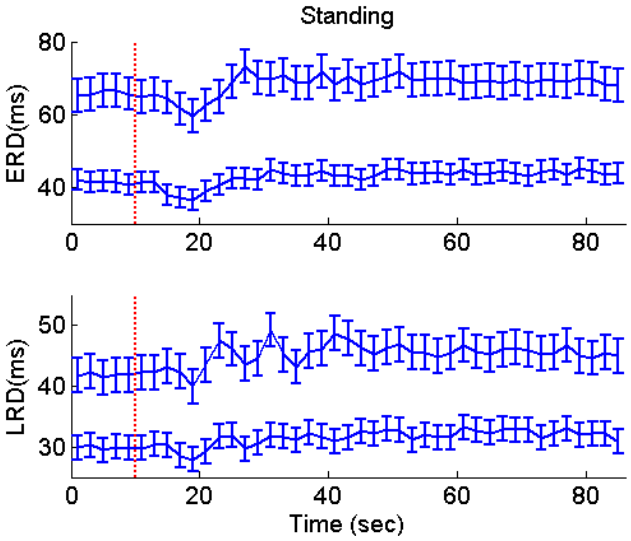

Figure 2: Plot of the median values of $ERD_{(30\%,50\%)}$ and $LRD_{(30\%,50\%)}$ with a 90% CI over 84 seconds. The postural change occurs at the dashed line at the 10 second mark.

4. Discussion and conclusions

4.1. Static

The RR and QT interval had significant differences between supine and standing. This is to be expected because of the increased sympathetic drive of the autonomic in response to the change from supine to standing posture. The rate-uncorrected QT interval was the longest when individuals were in supine position and shortest when they were standing (see Table 1).

All other parameters, besides $LRD_{70\%}$, did not yield any statistical difference between supine and standing two minutes after switching positions. This revealed their independence to body position changes and to different autonomic balance. However, one would note a trend toward a slight increase in duration in standing when compared to supine that did not reach significance (p=0.5).

$LRD_{70\%}$ for standing position was found significantly increased in comparison to the supine position (-12.30 ±37.35ms and p=0.013). One would note the larger standard deviation across the study population (37.35ms) which may reveal a low stability of this measurement or an increased variability of the terminal part of the T-wave in this position.

The RR and QT intervals were also found to be significantly different between supine and sitting (36.8±74.7ms and 12.4±11.3ms) but not as much as when comparing standing to supine positions (120±109ms and 16.2±14.9ms).

Even though there was a significant in QTcF between supine and standing, there was not such a difference with QTcB. The opposite was true when comparing supine and sitting. This observation emphasized the biased role of heart-rate correction formulas.

4.2. Dynamic

A change in body position leads to various changes in the heart and body. Some changes happen very rapidly while others occur over a longer period of time. The former will be referred as the early phase and the latter as the adaptation phase.

4.2.1. Early phase

After a person stands from a supine position there is an initial period where blood in the circulatory system begins to pool in the veins. This results in a reduction in the amount of blood returning to the heart and because of this a decrease in its contractive force. During this period of time, before the heart rate has changed, TpTe decreased by 15ms and $LRD_{(30\%)}$ was reduced by 2ms. One explanation could be that the changes in the contractive forces inside the ventricles have an effect on the electrical properties of the heart cells, which would then induce a change in the late part of the ventricular repolarization (quantified by TpTe and LRD parameters). It is also important to note that even though principle component analysis was used there could still be an effect due to changes in the hearts position of the body. We investigated the changes in T-wave amplitude in the scalar leads (X, Y and Z) and we found that even though there were changes in amplitude in these leads none of these signals corresponded with the changes seen in TpTe.

4.2.2. Adaptation phase

Following the rapid drop of TpTe interval duration the heart rate abruptly increases due to the decrease in blood

returning to the heart. As the heart rate increases TpTe increases to a value higher than it started. The explanation for this rapid change of TpTe interval following abrupt positional changes remains unclear. Previous studies have shown that TpTe is independent of heart rate [9], but these studies did not look at abrupt changes as described in our study. Our speculative explanation relies on the work described by Franz et al [10]. This group investigated the electrical and mechanical restitution of the heart at different rates of stimulation and they described different changes of the morphology of the monophasic action potential (MAP) of the myocardial cell in human for different pacing protocols: 1) during rapid changes in heart rate (abrupt changes) the late portion of the MAP is changed with an increased slope of the phase 3 (I_{Ks} changes) and 2) when the heart rate is changed progressively phase 2 of the MAP is prolonged while the phase 3 morphology is conserved (I_{Ks} does not change). This observation fits the concept that during postural changes the TpTe interval is changing with heart rate while later on, when the heart rate does vary slowly, the TpTe interval does not show any rate-related dependencies. Changes in MAP morphology are expected to impact the ventricular heterogeneity.

LRDs presented similar results to TpTe but to a smaller degree. Because LRDs are located in the same time interval as the TpTe interval, we believe that the same reasons that TpTe is changing apply to the changes in ERD and LRD.

Prolongation of the TpTe has been associated with an increase risk for ventricular arrhythmias [1]. Following our observations, a sympathetic burst may be associated with an increased prolongation of the terminal portion of the T-wave (increased ventricular heterogeneity) and represent a window of opportunity for arrhythmogenesis when additional proarrhythmic factors are present.

4.3. Conclusion

After the early and adaptation phases of ventricular repolarization have occurred there is still a significant change in heart rate and QT interval after sitting and standing. However, these changes in QT from postural changes alone are not clinically significant. TpTe, LRD and ERD were found to be unaffected by the same changes in body position.

TpTe, ERD, and LRD all had dynamic changes that occurred immediately after a postural change. It is believed that these changes could be due to changes in the contractive force of the heart as well as changes in phase 3 of repolarization. Changes in the TpTe interval were larger than the ERDs and LRDs and the reason for this is still unclear. These changes however occurred very rapidly and adjusted much faster than the QT interval.

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