# Characterization of the Temporal Evolution of the ECG Indices Under Abrupt Heart Rate Changes in Healthy Subjects

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*Abstract*— **Abnormal alterations in ventricular repolarization dispersion (VRD) have been shown to constitute a substrate for arrhythmias. In this work, we have induced abrupt heart rate (HR) changes to 17 healthy subjects through a Tilt-test and have analyzed the evolution of a set of ECG indices: Temporal ones (T-VRD), based on classic ECG intervals, and morphological ones (M-VRD), extracted features from an absolute T-wave. The quantification has been done by computing the alterations in index value and calculating their response time. In T-VRD indices, results have shown statistically significant decreases in T-wave onset-to-peak (*TOP*). Furthermore, these changes are responsible about the alterations in the T-wave width and in the *QT* interval. T-wave peak-to-end (*TPE*) has not shown statistical significance. Regarding M-VRD indices, we have observed that the shape of the T-wave undergoes to a fast initial reduction in amplitude and a posterior slow shifting toward the QRS-complex. The area of the both halves of the T-wave have shown statistically significant decreases, but relationship between themselves has remained practically constant. Finally, several ECG indices have reached the steady state before the RR interval. This study provides the normal range of VRD values in healthy young subjects during HR changes.**

*Keywords*— **ECG, T-wave morphology, ventricular repolarization dispersion, HR changes**

## I. Introduction

Ventricular Repolarization Dispersion (VRD) is usually associated to the electrical inhomogeneities in the cardiac repolarization process. It has been demonstrated in both human [1] and animal [2] models, that in presence of several cardiac diseases, abnormal alterations in VRD can be observed.

Experimental studies have shown that changes in T-wave width are correlated with alterations in VRD [3]. It has also shown that ECG T-wave widening can result from a differential shortening or lengthening of the action potential duration in both apex-base and transmural [2]. Some authors have suggested the T-wave peak-to-end interval as a marker of transmural dispersion [4, 5], and so, the T-wave peak as an indicator of the full repolarization of epicardium. Moreover, the correlation between *QT* interval and the changes in RR intervals has been established as a marker of cardiac risk [6]. However, some researchers have objected the validity of these two indices as markers of VRD [1, 7] and have questioned their dependence of HR [8]. It has also been suggested that several morphological indices, such as the slopes and the area of the T-wave, are independent of HR [9]. Finally, it has been shown that aging modulates the VRD [10].

In this study, we have analyzed how well ECG indices reflect changes in VRD under HR changes, with the aim of determine the range of normal values outside which we could assume that exists a risk of cardiac disease.

## II. Materials and Methods

### A. Data Set

The Autonomic Nervous System Database (ANS-UZ) has been acquired by the University of Zaragoza. Includes 17 healthy subjects with no previous cardiovascular diseases and with a mean age of $28.5 \pm 2.8$ years. Each subject recording has undergone a head-up tilt test trial according to the following protocol: 5 minutes in the supine position, 5 minutes tilted head-up to an angle of 70 degrees, and 18 seconds during table movement. This method generates an abrupt acceleration of the heart rate. The standard ECG leads I, III and the V1-V6 precordials were recorded during the whole test using the ECG100C module (Biopac, USA) with a sampling rate of 1000 Hz.

### B. ECG Preprocessing

The ECG signals have been preprocessed as follows: 1) QRS complexes have been detected and normal beats have been selected according to the method in [11], 2) A Butterworth high-pass filter (0.5Hz, bidirectional) has been applied

for baseline wander rejection and in order to reduce high frecuency noise, a Butterworth low-pass filter (100Hz, bidirectional) has been used, and 4) T-waves have been located and delineated using the wavelet-transform based method in [12].

We have applied a multilead criteria to determine wave boundaries, where $T_{\text{ON}}$ and $QRS_{\text{ON}}$ are respectively the earliest reliable T-wave and QRS-complex onset at any lead and $T_{\text{END}}$ is the latest reliable T-wave end in the I, III, V1-V6 leads, applying the rules presented at [13]. Also, the T-wave peak ($T_{\text{PEAK}}$) and R-wave peak ($R_{\text{PEAK}}$) as median values of all leads have been computed with an outlier protection rule [13].

### C. Ventricular repolarization dispersion indices

We have defined two kind of VRD indices: Temporal ones (T-VRD), related to typical ECG time intervals, and morphological ones (M-VRD), linked to T-wave shape.

In T-VRD indices, for each i$^{th}$ beat we have computed the following electrocardiographic intervals: The QRS-onset to T-wave-end interval (***QT***), quantifying the full depolarization and repolarization of ventricles; the T-wave width (***TW***), quantifying the total repolarization time; and finally the T-wave onset-to-peak interval (***TOP***) and the T-wave peak-to-end interval (***TPE***), which several authors have linked to the full repolarization of epicardium and transmural repolarization respectively [4]. The compute of these indices is shown in Equations 1, 2, 3 and 4.

$$QT_i = T_{\text{END}_i} - QRS_{\text{ON}_i} \tag{1}$$

$$TW_i = T_{\text{END}_i} - T_{\text{ON}_i} \tag{2}$$

$$TOP_i = T_{\text{PEAK}_i} - T_{\text{ON}_i} \tag{3}$$

$$TPE_i = T_{\text{END}_i} - T_{\text{PEAK}_i} \tag{4}$$

Regarding M-VRD indices, in order to extract all T-wave shape features, we have developed an algorithm which computes the contribution of the eight independent recorded ECG leads (I, III, V1-V6). As can be seen in Equation 5, we have generated a single T-wave (So called Absolute T-wave: $T^{\text{ABS}}$) through the absolute sum of the 8 T-waves in each i$^{th}$ beat.

$$T_i^{\text{ABS}}(k) = \sum_{j=\text{I,III,V1-V6}} |ECG(j,k)| \quad k = T_{\text{ON}_i}\ ,\ \ldots\ ,\ T_{\text{OFF}_i} \tag{5}$$

Finally, a polynomial fitting has been applied for each i$^{th}$ $T^{\text{ABS}}$, obtaning $\tilde{T}_i^{\text{ABS}}$ and the following M-VRD indices were calculated: T-wave Amplitude ($\boldsymbol{T_A}$), calculated as the amplitude of the $\tilde{T}_i^{\text{ABS}}$ wave peak; Slope of Early T-wave ($\boldsymbol{S_{ET}}$), maximum slope obtained through a five point centered derivative in whole first half of $\tilde{T}_i^{\text{ABS}}$ wave; Slope of Late T-wave ($\boldsymbol{S_{LT}}$), absolute value of the maximum slope obtained through the five point centered derivative in whole second half of $\tilde{T}_i^{\text{ABS}}$ wave; Areas of Early, Late and Total T-wave ($\boldsymbol{A_{ET}}$, $\boldsymbol{A_{LT}}$ and $\boldsymbol{A_T}$), surface under the curve of the first half, the second half and total $\tilde{T}_i^{\text{ABS}}$ wave respectively; and Proportion of Early and Total T-wave Area ($\boldsymbol{RA_{ETT}}$), relationship between first half and total surface under the curve of the $\tilde{T}_i^{\text{ABS}}$ wave.

### D. Temporal evolution of T-VRD and M-VRD indices

For each index, the values beat-to-beat have been concatenated and so obtained a serie of values over time. A numerical interpolation has been applied using the $R_{\text{PEAK}}$ values as time reference for all beats in order to resample to 1 Hz each index. For the sake of robustness, it has also been applied a median filter with a windows size of 20 seconds on all series of indices. Then, we have randomly selected multiple indices and have observed that all shown an abrupt initial change and a slower subsequent stabilization. These two phases of adaptation have also been previously observed in *QT* [14]. So, the temporal evolution has been characterized through a numerical fit with a linear combination of two exponentials, as shown in Eq. 6, where $a_0\ ,\ldots\ ,a_3$ are the fitting parameters.

$$\widetilde{f}_{(n)} = a_0 e^{a_1 . n} + a_2 e^{a_3 . n} \tag{6}$$

The optimization is based on the minimization of the sum of squared error of each serie, as illustrated in Equation 7 where $I_{(n)}$ represents the index under study.

$$\frac{\partial {e_r}^2}{\partial a_k} = \frac{\partial}{\partial a_k} \sum_{n=1}^{N} (I_{(n)} - \widetilde{f}_{(n)})^2 = 0 \tag{7}$$

Finally, we have quantified each index evolution through three parameters (see Fig. 1): Index value variation ($\Delta$), response time ($t_r$) (time between 10% and 90% of change) and initial delay ($\Theta_D$). The latter, is computed as the difference between starting points of the evaluated index and the Tilt-test Maneuver (obtained through the RR initial value).

### E. Population analysis

In order to reduce the intersubject variability, we have normalized for all subjects subtracting to the index its initial (0%) value (see Eq. 8). Then, we have compared the population in the 100% of the index change with the population reference (set to 5% of change) by applying a non-parametric

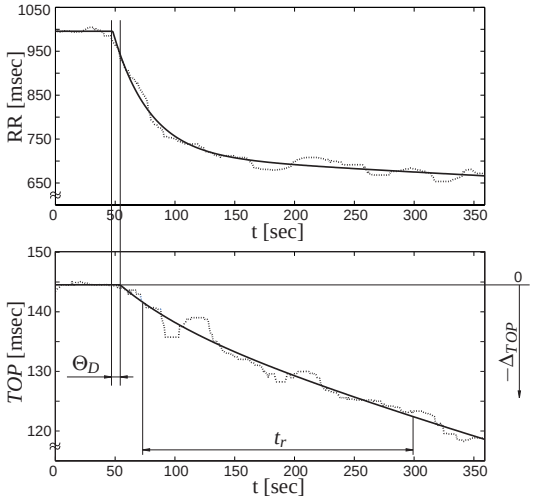


Fig. 1: Example of characterization. The dotted line shows the index value and bold line represents the fitting curve.

Table 1: Quantification of temporal values (Mean $\pm$ SD)

| Index | $t_r$ [sec] | $\Theta_D$ [sec] |
|---|---|---|
| RR | $112 \pm 81$ | - |
| *QT* | $105 \pm 62$ | $16 \pm 12$ |
| *TOP* | $156 \pm 46$ | $8 \pm 3$ |
| *TPE* | $72 \pm 47$ | $13 \pm 14$ |
| *TW* | $152 \pm 76$ | $12 \pm 7$ |
| $T_A$ | $65 \pm 59$ | $9 \pm 5$ |
| $S_{ET}$ | $28 \pm 15$ | $12 \pm 6$ |
| $S_{LT}$ | $41 \pm 31$ | $12 \pm 6$ |
| $A_{ET}$ | $114 \pm 57$ | $9 \pm 6$ |
| $A_{LT}$ | $86 \pm 65$ | $10 \pm 10$ |
| $A_T$ | $98 \pm 66$ | $8 \pm 7$ |
| $RA_{ETT}$ | $53 \pm 40$ | $14 \pm 7$ |

two-sided Mann-Whitney U test.

$$\Delta_I = I - I(0\%) \quad I \equiv Evaluated\ index \tag{8}$$

## III. Results

Except *TPE* and $RA_{ETT}$, all indices have shown significant alterations in their values in response to physiological changes induced by abrupt variations in HR. In Fig. 2, we have summarized all statistical results of both T-VRD and M-VRD. In T-VRD, we can see a significant decrease in $\Delta_{QT}$, $\Delta_{TW}$ and $\Delta_{TOP}$. The highest statistical significance has been found in $\Delta_{TOP}$. Regarding M-VRD indices, the most significant changes have been seen in $T_A$. Moreover, not all indices spend the same time to reach the steady state. In Table 1 we have shown $\Theta_D$ and $t_r$ values in Mean $\pm$ SD for all VRD indices. As can be seen, *TOP* is the first in begin to change but is which has the highest response time. Slope indexes have been the quickest in time response. It should be noted that several indices reach their steady state while RR is still changing.

## IV. Discussion

In the present study, we have described the dynamics of VRD through temporal and mophological indices. We have observed a statistically significant decrease of *QT* in response to RR decreases (see Fig. 2). This behavior has been detected previously by Pueyo et al. by evaluating 24-h 3-lead Holter ECG recordings [6]. Furthermore, other authors have proposed the T-wave width as a improved marker of VRD [2]. We have shown in this work that alterations in both *QT* and *TW* are caused by changes in *TOP* (index with highest statistical significance). The HR dependence of the latter has been previously found by Merri et al. in standard ECGs [9], but it has not by Andersen et al. in holter recordings [8]. The study of the characteristic times ($\Theta_D$ and $t_r$) allows us to suppose that the reason of the previous controversy has to do with different durations of the protocols of both group of researchers (i.e. since *TOP* changes slowly, a sufficient time to detect its change is required).

Regarding M-VRD indices, we have found statistically significant changes in $T_A$ and in T-wave slopes. These results agree with other studies [8]. The area of both halves of T-wave have shown significant decreases. However, $RA_{ETT}$ has remained practically constant. Furthermore, these changes reach the steady state faster than RR, which enables us to suppose that the reduction of their values has a physiological limit.

Our database consists of quasi-equal-aged subjects, and so, we have avoided the problem of aging modulation of VRD previously reported [10]. Finally, since it has been suggested that the T-wave peak coincides with full repolarization of epicardium [4], our findings point out that HR changes induce alterations mainly in the epicardial region.

## V. Conclusion

Since *TOP* has shown statistical significance and *TPE* has not, we have concluded that HR increases induce in the shape of the T wave a shift in the peak position towards the QRS-complex. In the same way, $T_A$, $S_{ET}$ and $S_{LT}$ have shown sig-

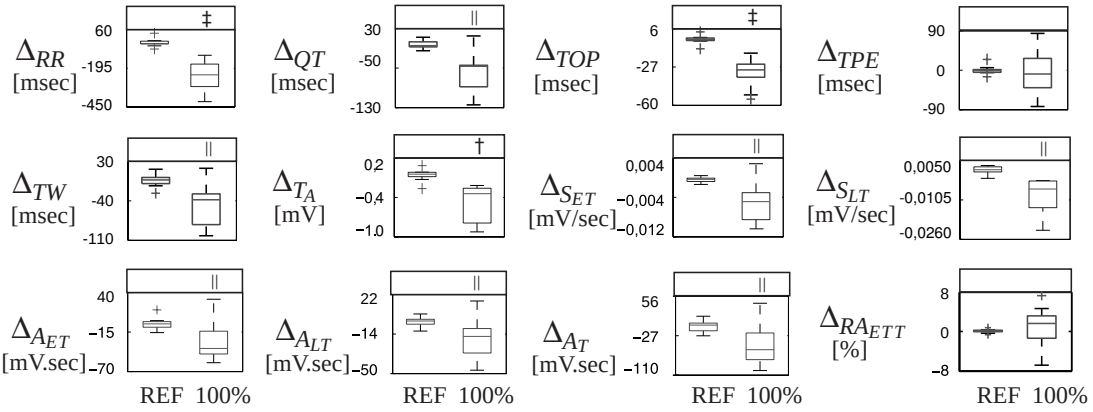


Fig. 2: Box and Whisker diagram for all VRD indices. Statistical significance was signed as '||' for p<0.005, '†' for p<0.0005 and '‡' for p<0.00005. A '+' mark indicates an outlier. The population reference "REF" is the 5% of change in index value respect to the intial state.

nificant decreases, thus HR increases induces a T-wave decrement in amplitude. These effects have a physiological limit because several indices reach the steady state before RR, i.e. some ECG indices have a less capability of changing than others. This study constitute a basis for setting normal conditions of the repolarization process. Further investigations are needed for determining the VRD alterations in non-healthy subjects and make a comparison with normal range of values.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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