Study of T-wave morphology parameters based on Principal Components Analysis during acute myocardial ischemia

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Abstract. Electrocardiographic repolarization abnormalities can be detected by Principal Components Analysis of the T-wave. In this work we studied the effect of signal averaging on the mean value and reproducibility of the ratio of the 2nd to the 1st eigenvalue of T-wave ($T_{21}^{W}$) and the absolute and relative T-wave residuum ($T_{ab}^{WR}$ and $T_{rel}^{WR}$) in the ECG during ischemia induced by Percutaneous Coronary Intervention. Also, the intra-subject and inter-subject variability of T-wave parameters have been analyzed. Results showed that $T_{rel}^{WR}$ and $T_{abs}^{WR}$ evaluated from the average of 10 complexes had lower values and higher reproducibility than those obtained from 1 complex. On the other hand $T_{21}^{W}$ calculated from 10 complexes did not show statistical differences versus the $T_{21}^{W}$ calculated on single beats. The results of this study corroborate that, with a signal averaging technique, the 2nd and the 1st eigenvalue are not affected by noise while the 4th to 8th eigenvalues are so much affected by this, suggesting the use of the signal averaged technique before calculation of absolute and relative T-wave residuum. Finally, we have shown that T-wave morphology parameters present high intra-subject stability.

1. Introduction
The electrocardiographic ventricular repolarization dispersion (VRD) can be evaluated by parameters based on the Principal Component Analysis (PCA) such as the ratio of the 2nd to the 1st eigenvalue ($T_{21}^{W}$) and either relative or absolute T-wave residuum ($T_{ab}^{WR}$ and $T_{rel}^{WR}$). These parameters, applied to 12-lead standard ECG quantify the spatial complexity of ventricular repolarization and may become a noninvasive diagnostic tool in different cardiac pathologies [1]. The aim of this work is to evaluate the PCA-based parameters derived from signal averages in ischemic patients. We hypothesize, according to the results of Batdorf et al. in healthy subjects [2], that the PCA-based morphology parameters obtained during ischemia in averaged ECG will present lower values and better reproducibility than when computed from a single beat. For that purpose, we evaluated VRD in the course of transmural ischemia induced by Percutaneous Coronary Intervention (PCI) procedure [3]. The balloon-inflation PCI provides an advantageous model of the first minutes of acute ischemia in humans, due to a total interruption of blood flow through the ventricles.
2. Materials and Methods

2.1. Data Set
The study group consisted of 93 ECG records from patients at the Charleston Area Medical Center in West Virginia undergoing elective prolonged balloon occlusion during PCI in one of the major coronary arteries (STAFF-III study) [3]. This group was selected from a total of 108 patients, with the condition that T-wave could be delineated during the complete time course of ischemia. The mean inflation duration was 4’ 28” with a standard deviation of 74”. Eight independent ECG leads (V1-V6, I, II) were recorded using equipment by Siemens-Elena AB (Solna, Sweden) and digitized at sampling rate of 1000 Hz and amplitude resolution of 0.6 μV. Leads III, aVR, aVL and aVF were derived from leads I and II. ECGs were acquired for each patient in supine position. Two control records \( C_k \) (\( k=1,2 \)) were continuously acquired for 5-minute some time before the PCI and one ECG was recorded during PCI.

2.2. ECG processing
For a total of 93 patients, the 8 ECG leads were processed in control situation and PCI procedure respectively. The QRS fiducial points were detected on a multilead basis by an automatic QRS detector [4]. Cubic spline interpolation was used for baseline wander rejection and the ECG delineation system based on the Wavelet Transform has been used for T-wave location and delineation [5].

We analyzed the morphological T-wave parameters for both single complex (1-Cx) and average of 10 complexes (10-Cx) using Singular Value Decomposition (SVD). First of all a “template beat” was calculated. For that purpose 10 beats were segmented using a constant window and aligned using a cross-correlation technique. After that the template beat was obtained through direct averaging of 10 beats. Second new jitter-corrected beats (arising from analysis windows) were used into the “final average beat” if the cross-correlation coefficient between the new beats and the “template beat” in each channel was greater than 98%, otherwise the beat is rejected. Two rejected beats were the accepted limit on the computation of each \( i^{th} \) “final average beat”. The cross-correlation coefficient was calculated from the QRS, which was segmented by taking a 200 msec. interval centered at the QRS-fiducial point previously detected [4] [6].

The computation of T-wave morphological parameters, calculated from 1-Cx and 10-Cx, were obtained from onto N-samples windows (\( W_i \)), which defines ventricular repolarization phase for the \( i^{th} \) beat of ECG. The beginning of these windows was calculated as a median value of T-wave onset in the 8 independent ECG leads. In the same way, the end of these windows was obtained with the median value of T-wave offset fiducial points. Afterward SVD was applied obtaining one set of 8 singular values \( \xi_j \) (\( j = 1,\ldots,8 \)), which are ordered such that \( \xi_1 \geq \xi_2 \geq \xi_3 \geq \ldots \geq \xi_8 \geq 0 \). SVD technique finds a system of eight orthogonal directions (S1...S8), in which S1 contains most of the ECG energy, S2 contains most of the remaining ECG energy, and so forth. It has been shown that the first three directions S1 S2 S3, contain 98 % of the whole ECG energy [7] representing the dipolar component, while the last 5 represent the so-called non-dipolar components of the T-wave respectively. In this sense, we have computed and evaluated the T-wave morphology parameters based on PCA; these parameters have been named \( T \) parameters and were calculated as:

- The ratio of second to the first eigenvalue for the \( i^{th} \) beat, corresponding with the T-wave, expressed as:

\[
T_{W_i}^{21} = 100 \ast (\xi_{i,2}^2/\xi_{i,1}^2)
\]
Figure 1. The effect of using a single complex versus 10 complex signal average on the mean±SEM (standard error mean) in control and during PCI procedure. (A) Absolute T-wave residuum, (B) Relative T-wave residuum and (C) the ratio of second to the first eigenvalue. 1-Cx (blank circle) and 10-Cx (filled circles). Control Situation (C), first minute of occlusion (O₁), second minute of occlusion (O₂) and the third minute of occlusion (O₃).

- The absolute T-wave residuum, for the $i^{th}$ beat, to quantify the non-dipolar components as the sum of the fourth to the eight eigenvalues, calculated as:
\[ T_{WR_i}^{abs} = \sum_{l=4}^{8} \xi_{i,l}^{2} \] (2)

- The relative T-wave residuum, for the \( i \)th beat, to quantify the relative contribution of \( T_{WR_i}^{abs} \) with respect the total energy, calculated as:

\[ T_{WR_i}^{rel} = 100 \times \left( \sum_{l=4}^{8} \frac{\xi_{i,l}^{2}}{\sum_{l=1}^{8} \xi_{i,l}^{2}} \right) \] (3)

The \( T \) parameters, \( T_{WR_i}^{abs}, T_{WR_i}^{rel} \) and \( T_{W}^{21} \), were obtained from a single complex and from the 10 complexes in the signal averaging.

2.3. Statistical analysis

We analyzed the statistical distribution of \( T \) parameters using D’Agostino-Pearson normality test. The \( T \) parameters, in both control and PCI procedure, did not follow a Gaussian distribution. Therefore, a two-tailed non-parametric Mann-Whitney test and Wilcoxon Signed Rank Test were applied. When \( p \) value was <0.05, differences were considered statistically significant.

2.4. Intra-individual variability of \( T \) parameters

To assess the intra-individual variability of \( T \) parameters [8], the standard deviation (SD) of \( T \) expressed as \( \xi_{k}^{T}(j) \) was computed for each patients \( (j = 1, \ldots, J) \) in each of the two control ECG recordings \( C_{k}, k = 1, 2 \). Also, the difference between SDs of the two control recordings was calculated as: \( D^{T}(j) = \xi_{1}^{T}(j) - \xi_{2}^{T}(j) \). Then, the Wilcoxon Signed Rank Test was applied to the difference \( D^{T}(j) \) from the total of population and \( T \) parameters, with the aim to evaluate the next hypothesis:

- \( H_{0} \): the intra-individual change is zero
- \( H_{1} \): the intra-individual change is different to zero

2.5. Inter-individual variability of \( T \) parameters

To assess the inter-individual variability of \( T \) parameters [8], the mean value of the two SDs \( \xi_{k}^{T}(j), (k = 1, 2) \), was calculated as \( \xi_{j}^{T} = \frac{1}{2} \{ \xi_{1}^{T}(j) + \xi_{2}^{T}(j) \} \). Then SD of \( \xi_{j}^{T}(j) \) over all patients \( (j = 1, \ldots, J) \) was denoted by \( \chi_{j}^{T} \). Moreover, the SD of the two SDs \( \xi_{k}^{T}(j), k = 1, 2 \) for each patient \( j \) was computed and denoted by \( \chi_{k}^{T} \).

The Wilcoxon Signed Rank Test was applied to compare intra-individual variability \( \chi_{j}^{T} \), for \( j = 1, \ldots, J \), with the inter-individual SD of the whole population \( \chi_{\Sigma}^{T} \).

3. Results

The series \( T_{WR_i}^{abs}, T_{WR_i}^{rel} \) and \( T_{W}^{21} \) were calculated during control and balloon inflation in PCI procedure and, for the sake of robustness, it was applied a median filter with a windows size of 7.5 sec on the three series of parameters. We characterized 4 different time instants: \( T \) parameters during Control Situation (\( C \)) (mean value of \( C_{k}, k = 1, 2 \)) associated to the median value of 5 minutes just before the start of occlusion, \( T \) parameters during the first minute (\( O_{1} \)) associated to the median of 7.5 sec centered around the first minute, the second (\( O_{2} \)) and the third (\( O_{3} \)), for their respective minutes of the occlusion procedure.

Table 1 shows the results represented by the mean value ± of the Standard Error of the Mean (SEM) of \( C, O_{1}, O_{2} \) and \( O_{3} \) values for each \( T \) parameter considering the 93 analyzed records. The results showed that \( T_{WR_i}^{abs}, T_{WR_i}^{rel} \) and \( T_{W}^{21} \) values during PCI compared against control situation...
Table 1. Mean values ± SEM of $T$ parameters. $^A p<0.001$ and $^B p<0.0001$ against control. $^C p<0.0001$ represent significant differences between 10-Cx and 1-Cx.

<table>
<thead>
<tr>
<th></th>
<th>Cx</th>
<th>$T_{\text{abs}}^\infty$ (mV²)</th>
<th>$T_{\text{rel}}^\infty$ (%)</th>
<th>$T_{21}^\infty$ (%)</th>
</tr>
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<tbody>
<tr>
<td>1C</td>
<td>0.087±0.007</td>
<td>0.18±0.026 $^A$</td>
<td>0.211±0.029 $^A$</td>
<td>0.200±0.023 $^A$</td>
</tr>
<tr>
<td>10C</td>
<td>0.012±0.001 $^C$</td>
<td>0.037±0.004 $^{C,B}$</td>
<td>0.046±0.004 $^{C,B}$</td>
<td>0.041±0.004 $^{C,B}$</td>
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<table>
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<tr>
<th>Cx</th>
<th>$T_{\text{rel}}^\infty$ (%)</th>
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<tbody>
<tr>
<td>1C</td>
<td>0.29±0.04 $^A$</td>
</tr>
<tr>
<td>10C</td>
<td>0.05±0.01 $^C$</td>
</tr>
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<table>
<thead>
<tr>
<th>Cx</th>
<th>$T_{21}^\infty$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1C</td>
<td>5.92±1.07 %</td>
</tr>
<tr>
<td>10C</td>
<td>3.80±0.45 %</td>
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</tbody>
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Table 2. Reproducibility estimated as SDs of within-subject variance of $T$ parameters. $^* p<0.0001$ represents significant differences between 10-Cx and 1-Cx.

<table>
<thead>
<tr>
<th>Cx</th>
<th>$T_{\text{abs}}^\infty$ (mV²)</th>
<th>$T_{\text{rel}}^\infty$ (%)</th>
<th>$T_{21}^\infty$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.027</td>
<td>0.09</td>
<td>1.27</td>
</tr>
<tr>
<td>10</td>
<td>0.004*</td>
<td>0.01*</td>
<td>0.99</td>
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Figure 2. One example (patient number 10) of time evolution of $T$ parameters for both 1-Cx (dotted line) and 10-Cx (black line) during PCI procedure. The vertical lines represents the start and end of occlusion.
were statistically significant for 1-Cx as well as 10-Cx analysis. Also we have studied the effect of ECG signal averaging vs. a single complex. The results shows that $T_{WR}^{abs}$ and $T_{WR}^{rel}$ values for 1-Cx compared against 10-Cx value are statistically significant, for both control and during PCI procedure. However, non significant differences were found for $T_{W}^{21}$ parameter.

The mean value ± SEM of $T$ parameters are plotted in Figure 1, also it can be observed that T-wave morphological parameters show an increased tendency during PCI.

Table 2 shows standard deviations (SDs) of within-subject variance of $T_{WR}^{abs}$, $T_{WR}^{rel}$ and $T_{W}^{21}$. For minute-to-minute observation intervals of control situation we have observed significantly less variance for both $T_{WR}^{abs}$ and $T_{WR}^{rel}$ as the quantities of complexes were increased from 1 to 10. We have not observed $T_{W}^{21}$ statistically significant differences between 1-Cx to 10-Cxs respectively. In Figure 2 we show time-course evolution of $T_{WR}^{abs}$, $T_{WR}^{rel}$ and $T_{W}^{21}$ during PCI procedure (patients #10).

A high intra-individual stability of $T$ parameters was obtained (Section 2.4). The $p$ value of the Wilcoxon Signed Rank Test was $<0.05$ and the hypothesis $H_0$ of the intra-individual variability being negligible was accepted. Moreover, the inter-individual variability of $T$ parameters was obtained (Section 2.5). The Wilcoxon Signed Rank Test showed that, the differences between intra-individual variations $\chi^{T\leftrightarrow}_{k}(j)$ and SD of the whole population $\chi^{T\leftrightarrow}$ were highly significant ($p<0.05$), being $\chi^{T\leftrightarrow} > \bar{\chi}^{T\leftrightarrow}_{k}$; where $\bar{\chi}^{T\leftrightarrow}_{k} = \frac{1}{J} \sum_{j=1}^{J} \chi^{T\leftrightarrow}_{k}(j)$.

4. Discussion and conclusions

We have hypothesized that $T$ parameters obtained from ECG signal averaging with 10 complexes would have lower mean values and more reproducibility than those derived from a single complex analysis during control and PCI procedure. The obtained results indicate that:

1) $T_{WR}^{abs}$ and $T_{WR}^{rel}$ computed from 10-Cx show lower values, and higher reproducibility than those obtained from 1-Cx. This results suggest that a big amount of absolute and relative T-wave residuum on one beat is due to noise.

        However $T_{W}^{21}$ computed on the average cycle did not show statistical significant with respect to $T_{W}^{21}$ on single beats; possibly because the numerator of $T_{W}^{21}$ (2nd eigenvalue) is not so much affected by noise as it is the numerator of relative T-wave residuum; obtained from the smaller 4-to-8 eigenvalues.

2) The results were obtained as from control situation (corresponding to patients with cardiac disease) and PCI (corresponding acute ischemic process). The results observed were concordant with the study from healthy subject done by Batdorf et al. [2].

3) The results showed that signal averaging technique can provide more significant differences than a single complex analysis. The ECG ventricular repolarization dispersion parameters (i.e, both relative or absolute T-wave residuum) can be improved through the use of signal-averaged technique.

4) Intra-individual analysis showed that the $T$ parameters variability have high stability in control recordings. Moreover, the inter-individual analysis showed that the $T$ parameters should be normalized in order to diminish such variation.

On the other hand, we have found the following limitations for this study. Batdorf et al. [2] shows that 200 complexes of signal averaging have lower noise and higher reproducibility than 10 complexes of signal averaging. In this work we did not increase the beats quantity into the signal average technique because dynamic ST-changes during PCI could be affected the measure of T-wave morphology. Furthermore, we have observed increases in noise of the ECG during PCI procedure, a phenomenon that should be quantified for different stages of the angioplasty procedure. Then, future studies are needed to investigate the optimal and maximum beats number that it is feasible to include into the average technique for PCI studies; as well as a
method of normalization to reduce the variability between subjects. Also, we have analyzed the normal reproducibility or dispersion in $T_{abs}$, $T_{col}^W$, and $T_{rel}^W$ during five minutes.

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References