T wave alternans detection: A simulation study and analysis of the European ST-T Database

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Abstract

The detection of T wave alternans (TWA) in surface ECG signals has been recognized as a marker of electrical instability, and is hypothesized to be related with patients at increased risk for ventricular arrhytmias. In this paper we present a evaluation study of a method for detecting ST-T complex alternans based on the Complex Demodulation approach (CD), and the application of the detector to the European ST-T Database. To study the performance of this detector, a simulated ECG signal was obtained adding controlled alternans to a database of young, healthy subjects ECGs. In this way, the ECG signal contained noise and non-alternans ST-T variability coming from real recordings. The detector applied to the European ST-T Database (where ischemic ST and T episodes were manually annotated by physicians), detected 148 TWA episodes, from which 82 (55.4 %) overlapped with ischemic episodes, while in 12.0% of the annotated ischemic episodes, a TWA was detected. A significant correlation between ST elevation and the existence and magnitude of TWA was found.

1 Introduction

Sudden cardiac death (SCD) is the leading cause of cardiovascular mortality in the developed countries [1]. There is not an effective diagnostic method to identify patients at high risk for SCD. All the the non-invasive tests related to high-risk SCD (ventricular arrythmias in 24-hour Holter monitoring, ventricular late potentials, low heart rate variability, dispersion of repolarization...) lack the sufficient positive predictivity to make a decision about specific treatment, especially defibrillator implantation. Nowadays, the challenge is to develop new selective non-invasive methods which will allow the identification of high-risk patients before they experience major arrythmic events.

Electrical T-wave alternans (TWA) is defined as a consistent fluctuation in the repolarization morphology which repeats on every-other-beat basis. TWA have been documented in a wide range of experimental and clinical situations, such as long QT syndrome, myocardial ischemia and infarction, coronary artery occlusion, Printzmetal angina and several other pathologic conditions.

Although visible TWA is an infrequent phenomenon, in recent years, computerized analysis of digital ECG recordings allowed the identification of subtle and non-visible (microvolt) TWA, much more common than visible TWA.

Several methods for TWA detection have been proposed. All of them are based on the well-known problem of spectral estimation. The spectral method [2] used the FFT to analyze the frequency component 0.5 cycles/beats over the aligned ST-T complexes. This method assumes stationarity of TWA episodes and yields an average measure of T-wave alternans over the analysis window. The TWA is considered as "present" or "not present".

In the complex demodulation approach (CD) [3] TWA is modeled as a sine wave at 0.5 cycles/beat, with varying amplitude and phase. The aligned ST-T complexes are demodulated and low-pass filtered to obtain a continuous beat-to-beat alternans measurement.

More recently several global methods have been applied that consider the repolarization as a whole, instead of using a independent analysis for each sample of the ST-T complex, based on Karhunen-Loève transform [4] and on the correlation with a median beat [5].

In a previous work [6] we compared the performance of all these methods with signals composed of a repeated beat plus noise and simulated TWA episodes. We studied the sensibility, positive predictivity and accuracy of the estimated amplitude, and concluded that filtering methods like Complex Demodulation and Capon high-pass filtering obtained the best results. As CD method was computationally less complex, we selected it for the present work.

The aim of this paper is twofold: to analyze the performance of a TWA detector on actual ECG recordings, and to study the relationship between ischemia and TWA, applying the detector to the European ST-T Database.

2 Materials and methods

2.1 TWA detection method

The proposed method is based on the CD approach [3]. The method has three different blocks: preprocessing, spectral estimation and thresholding.

First of all, QRS detection is needed. "Aristotle" software [7] was used for this purpose. Then, baseline wander was estimated and suppressed by means of cubic spline interpolation. Frequency components above those associated with the repolarization were attenuated using a 20th-order equiripple linear phase FIR low-pass filter with transition band between 15 and 30 Hz.

Finally, the ST-T complexes were segmented by selecting intervals of 300 ms, beginning at a variable distance b_k from the QRS fiducial point dependent on the RR interval. For the *k*-th beat

$$b_k = 40 + 1.3\, RR_k^{1/2} \text{ (all in } ms). \quad (1)$$

From the aligned ST-T complexes a matrix $\underline{\underline{x}}$ can be derived, where the element $x[k,l]$ is the l-th sample of the ST-T complex of the k-th beat. The rows of $\underline{\underline{x}}$ are the complexes and the columns of $\underline{\underline{x}}$ are time series where beat-to-beat changes in repolarization can be found.

Once the matrix $\underline{\underline{x}}$ is built, the aim of the detector is to quantify the power spectrum of the signal at the frequency of alternation $f_o = 0.5$ cycles/beat. Each column of $\underline{\underline{x}}$ is demodulated so that the frequency components around f_o are moved to low frequencies:

$$y[k,l] = x[k,l] \cdot 2 \cdot \exp\left(j \cdot 2\pi f_o \cdot k\right) \quad (2)$$

and then the columns of the new matrix $\underline{\underline{y}}$ are low-pass filtered to get only the alternation components

$$z[k,l] = y[k,l] \star h_{LP}[k] = \sum_m y[m,l] \cdot h_{LP}[k-m] \quad (3)$$

where $h^{LP}[k]$ is the impulse response of the low-pass filter. The rows of the matrix $\underline{\underline{z}}$ are the alternans waveforms detected by the CD method. To quantify them, two time series were created

$$V_{alt}^{rms}[k] = \sqrt{\frac{1}{L}\sum_{l=0}^{L-1} z^2[k,l]} \quad (4)$$

$$V_{alt}^{max}[k] = \max\left(|z[k,l]|\right) \quad (5)$$

which are respectively, the RMS and the maximum value of the TWA amplitude along the *k*-th ST-T complex. In our implementation, we have made use of a high-pass filter with impulse response $h_{HP}[k] = h_{LP}[k] \cdot \exp\left(j\pi k\right)$, because, as it can be easily shown, if $f_o = 0.5$ cycles/beat, $|z[k,l]| = |x[k,l] \star h_{HP}[k]|$. The filter we used was a 11th-order Kaiser window FIR filter ($\beta = 0.5$) with half-power cutoff frequency equal to 1/40 cycles/beat.

As the columns of the matrix $\underline{\underline{x}}$ are linearly filtered, special care must be taken to identify and suppress beats with different morphology and very noisy beats, because their energy would be spread by the filtering causing distortion in TWA amplitude series and possibly generating false positive episodes. To avoid this, 4 kinds of beats are marked and replaced by a linear interpolation between the previous and later non-marked beats: (a) beats not annotated as normal by the QRS detection software, (b) beats with RR changes, (c) beats with a substantial change in the baseline and (d) beats with low estimated SNR.

The outputs of the CD method are beat-to-beat series of voltages. To define the onset and offset of TWA episodes a final stage based on an adaptive amplitude threshold combined with a time duration threshold was applied to $V_{alt}^{rms}[k]$. The amplitude threshold accounts for slow drift changes in TWA amplitude estimation by applying an exponential averager that defines the baseline for the TWA amplitude series. The baseline is estimated adaptively only from those beats considered as non-alternans by the detection algorithm.

2.2 Simulation study

In actual ECG recordings, the exact value and timing of the TWA episodes are unknown. Thus, we propose a simulation study to evaluate the TWA detector performance. In [6] the simulated alternans ECG signal was synthesized as a repetitive beat to which different kinds of noise and alternans episodes were added.

In order to take into account the ST-T complex non-alternans variations normally observed in real recordings, we made use of ECG recordings from young, healthy subjects (which were assumed not to present significative TWA), to which alternans episodes were added.

Twenty-three recordings from the Politecnico di Milano's database [8] were used in the simulation (sampled at 500 Hz, 5 μV/ADU). Each of them is about 30 minutes long and contains three orthogonal leads (X, Y and Z). In every recording, 20 alternans episodes were added to each lead. The episodes had a triangular-shaped evolution and a duration of 31 beats, while the TWA waveform added to each ST-T complex was a Hanning window, as shown in Figure 1. Finally, the TWA detector was applied, and the detected episodes were compared with the simulated ones. The simulation was repeated for different RMS amplitudes at the peak of the TWA episodes, ranging from 25 to 300 μV.

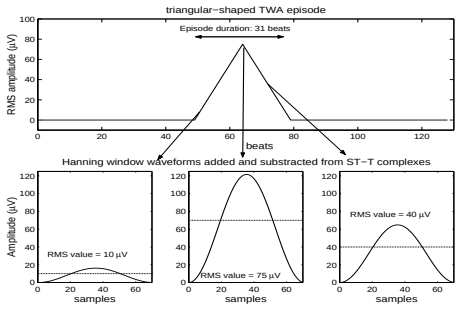

Figure 1: *Simulated TWA episodes and waveforms.*

To quantify the detector performance measurements, simulated and detected TWA episodes are compared, in terms of sensitivity S, defined as the number of correctly detected episodes divided by the total number of simulated episodes and the positive predictivity $P+$, calculated as the number of detected episodes that matched simulated episodes divided by the total number of detections. To consider matching between two episodes (simulated and detected) it is required that one episode contains at least half of the duration of the other.

2.3 The European ST-T Database

The *European ST-T database* [9] consists of 90 ECG recordings, each of two hours of duration, extracted from Holter tapes (2-lead ECGs) that contain ST-T complex episodes annotated on an individual lead basis by cardiologists. This database was chosen by two reasons: firstly, previous studies found T-wave alternans episodes [4], some of them related to annotated ischemic episodes. Secondly, this database is well-known and available by many research groups. The aim of the study was to know better the relationship between TWA and ischemia.

3 Results

3.1 Simulation results

In Table 1 we present the Sensibility (*S*) and Positive Predictivity (*P+*) of the detector applied to all the simulated ECG fragments (1380 episodes). Different amplitude threshold values were considered, showing that 15 μV above the baseline estimated amplitude was a reasonable option for this case. As for the temporal threshold, a minimum duration of 15 beats was demanded for an episode to be considered, to avoid spread spurious beats being considered as alternans episodes. As the signal of lead Y presented generalized episodes of motion artifacts in most of the recordings of the database, we show also in the table the *S* and *P+* over leads X and Z (excluding lead Y).

Table 1: *S and P+ values for different TWA amplitudes.*

	All leads		Leads X, Z	
TWA amp.	*S* (%)	*P+* (%)	*S* (%)	*P+* (%)
25 μV	61.3	88.8	82.2	98.1
50 μV	84.9	91.7	99.0	98.3
100 μV	93.3	92.5	99.7	97.8
150 μV	95.9	92.4	99.7	97.8
200 μV	97.3	92.2	99.7	97.8
300 μV	97.8	92.8	99.8	97.7

Results in Table 1 indicate that with the CD approach, T wave alternans above 50 μV can be mostly detected in all Holter leads (X,Y,Z), and acceptable results are obtained at cleaner leads for TWA amplitude $\geq 25\ \mu V$.

3.2 Results on the European ST-T Database

Applying the TWA detector to the entire ST-T database, the relationship between TWA and ischemic episodes can be analyzed. If we define:

- *I*: Total number of ischemic episodes at the database (T and ST episodes are combined with a logical OR).
- *A*: Total number of TWA episodes at the database.
- A_I: Number of TWA episodes overlapping ischemic episodes.
- I_A: Number of ischemic episodes overlapping TWA episodes.

Note that A_I is not necessarily equal to I_A, because of the possibility that there is not a one-to-one correspondence between TWA and ischemic episodes (e.g. two TWA episodes can be detected within an ischemic episode). Results are shown in Table 2 for episodes as well as for the number of beats belonging to each of these categories.

Table 2: *Relationship between detected TWA and annotated ischemia in ST-T Database.*

	I	A	A_I/A	I_A/I
Episodes	392	148	55.4 %	12.0 %
Beats	218814	7317	59.5 %	2.0 %

We found that 55.4% of the 148 detected TWA episodes were associated with ischemia whereas a TWA was found within a 12 % of the ischemic episodes. In the same table, the number of beats belonging to these categories are also given. As it can be seen, above 50% of the TWA episodes or beats were found during ischemic events. Moreover, the fact that overlapping beats are only 2% of ischemic beats, while 12% of the ischemic episodes do overlap, indicates that TWA episodes are shorter than ischemic ones.

We classified the detected TWA in two groups: those associated and not associated to an annotated ischemia in the same lead (A_I and $A_{\overline{I}}$). Along each episode, we calculated the RMS value of the TWA amplitude series $V_{alt}^{max}[k]$. The value of this parameter in the first group was 91.1$\pm$8.9 μV (*mean* $\pm$ *S.E.M.*), while for alternans not associated with ischemia, the RMS of $V_{alt}^{max}[k]$ was significantly lower: 71.3$\pm$3.4 μV (p = 0.04). Similarly, the maximum ST deviation of ischemic episodes associated with TWA was 355.1$\pm$32.3 μV, and that of those not associated with TWA was 199.3$\pm$9.3 μV ($p = 2{\cdot}10^{-5}$). Therefore, ischemic events with TWA showed significantly larger ST deviations.

In Figure 2, maximum TWA amplitudes are plotted against the maximum ST deviation for all overlapping episodes (I_A). A linear regression analysis yielded a correlation coefficient $r = 0.91$, showing a tendency for higher alternans to be associated to more severe ischemia.

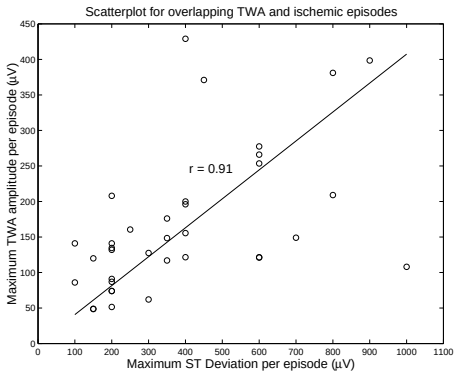

Figure 2: *Scatterplot of TWA maximum amplitudes vs maximum ST deviation in ischemic episodes overlapping TWA.*

Finally an example is given in Figure 3 where we can observe that 6 out of 7 ischemic episodes have a TWA episode inside them. In this record, all TWA episodes overlap with longer ischemic events. This behaviour agrees with results in Table 2. Moreover, most of the TWA episodes occur at the maximum ST deviation.

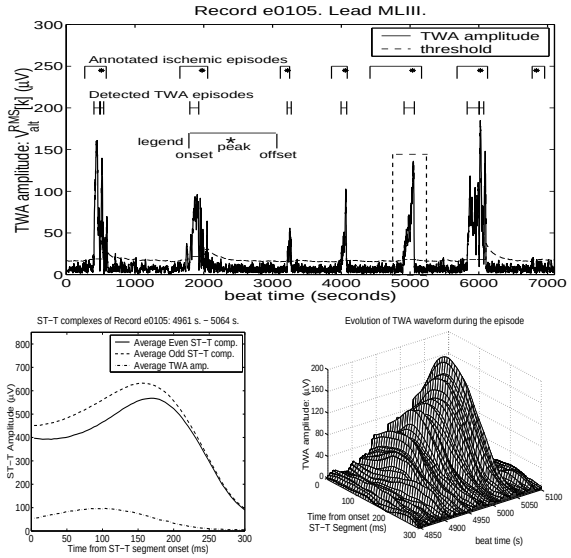

Figure 3: *Top: Example of $V_{alt}^{rms}[k]$ series for record e0105, showing the annotated ischemic episodes, detected TWA, and the adaptive threshold. Bottom: mean ST-T complexes and TWA (left) and TWA waveform evolution (right) of the episode marked with a dotted box in the top pannel.*

4 Conclusions

A TWA detector based on Complex Demodulation approach have been tested with Holter ECG signals containing simulated alternans. The results of the simulation indicated that the detector's performance is suitable in ambulatory recordings for TWA amplitudes larger than 50 μV.

The detector was applied to the European ST-T Database, showing that half the TWA appeared during longer ischemic events. The results suggest that the presence and amplitude of TWA during ischemia are clearly related with the severity of the ischemia.

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