T-Wave Alternans Quantification: which Information from Different Methods?

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Abstract

T-wave alternans, qualitatively defined as every-other-beat alternations of the T-wave morphology, has no standardized quantitative definition yet. Differences in quantitative information provided by the fast-Fourier-transform spectral method (FFTSM), the modified-moving-average method (MMAM), and our heart-rate adaptive match filter method (AMFM) were analyzed here making use of two synthetic ECG tracings with stationary TWA: triangular the first (TRI_TWA), with T-waves maximum-amplitude difference (A_{MAX}) of 100 μV and mean-amplitude difference (A_{MEAN}) of 50 μV; and uniform the second (UNI_TWA), with A_{MAX}= A_{MEAN}=100 μV. Application of FFTSM, MMAM, and AMFM to TRI_TWA yielded 57 μV, 100 μV, and 50 μV TWA amplitude estimation, respectively. Instead, 100 μV TWA amplitude was provided by each method after their application to UNI_TWA. Thus, FFTSM and AMFM provide estimates of A_{MEAN}, while MMAM of A_{MAX}.

1. Introduction

In the last decades, microvolt T-wave alternans (TWA) has been recognized as a non-invasive heart test to identify patients at increased risk of malignant ventricular arrhythmias and sudden cardiac death [1-5]. To this aim, several techniques for automatic TWA identification have been proposed in the literature [6-9], all based on the definition of TWA as every-other-beat changes in the T-wave amplitude and/or morphology. This generic TWA definition, however, does not allow quantitative comparison of results from different identification methods, which would rather require a preliminary standardization of technical specifications for TWA parametric characterization. In the absence of such technical standards, any correct comparison among quantitative outputs provided by different methods requires knowledge of the differences in the TWA parameterization at the basis of their algorithms. Differences in TWA quantitative information provided by the fast-Fourier-transform-spectral method (FFTSM) [6], the modified moving-average-method (MMAM) [7], and our heart-rate adaptive match filter method (AMFM) [8] were analyzed in the present study making use of two synthetic ECG tracings affected by stationary TWA with triangular and uniform profiles [10].

2. Methods

2.1. Quantitative definitions of TWA

In the clinical cases, TWA can be characterized by different profiles [10] (i.e. by different trends of the absolute amplitude difference between two consecutive T waves along the time axis), and any parameter relative to them may be considered for a quantitative definition of TWA. Two quantitative definitions of TWA were considered here: the maximum-amplitude difference (A_{MAX}), and the mean-amplitude difference (A_{MEAN}), defined as the maximum and the mean value of the TWA profile over time, respectively.

2.2. Simulated data

A basic ECG tracing was synthesized as a 128-fold repetition of a single noiseless beat extracted from a real ECG recording (sample frequency = 200 Hz, RR interval = 0.75 s). Two ECG tracings affected by stationary TWA were then derived from the basic one by changing every other T-wave amplitude according to: a) a triangular profile (TRI_TWA), characterized by an alternation mostly localized around the T-wave apex (A_{MAX}=100 μV and A_{MEAN}=50 μV); and b) a uniform profile (UNI_TWA), characterized by an alternans uniformly distributed along the T wave (A_{MAX}= A_{MEAN}=100 μV).

A graphical representation of TRI_TWA and UNI_TWA is shown in Fig.1A and Fig. 1D, respectively. Two superimposed consecutive T waves these ECG tracings are shown in Fig.1B and Fig. 1E, respectively, whereas the corresponding TWA profiles are shown in Fig.1C and Fig. 1F, respectively.

2.3. TWA Detection methods

Fast-Fourier-transform spectral method (FFTSM) [6]. According to this technique, beat-to-beat fluctuations in the electrocardiographic T-wave amplitude are measured using a spectral approach. After having aligned the N (N=128 for the simulated tracings) electrocardiographic complexes, a power spectrum, obtained as the squared magnitude of the fast Fourier transformation, is computed for each sequence of corresponding T-wave samples. Power spectra relative to all T-wave samples are then summed to obtain a cumulative spectrum, whose peak amplitude, at 0.5 cycle per beat, is called 'alternans peak', and is considered significant if the alternans ratio, AR, defined as:

$$AR = \sqrt{\frac{\text{alternans peak} - \mu_{noise}}{\sigma_{noise}}} \quad (1)$$

is greater than three. In equation (1), μ_{noise} and σ_{noise} are the mean and the standard deviation values of the spectral noise estimated in a predefined noise window. When the AR is significant, a measure of the TWA amplitude is provided by the FFTSM as follows:

$$A_{FFTSM} = \sqrt{\frac{\text{alternans peak} - \mu_{noise}}{N_S \cdot N}} \quad (2)$$

where N_S is the number of sample points in a T-wave window.

Modified-moving-average method (MMAM) [7]. This approach discriminates ECG beats between even beats, or beats A, and odd beats, or beats B. Then, modified-moving-average computed beats A and B are obtained by averaging alternate ECG beats as follows:

$$\begin{aligned} A_j(i) &= A_{j-1}(i) + \Delta_A \\ B_j(i) &= B_{j-1}(i) + \Delta_B \end{aligned} \quad (3)$$

where the j and i notations are respectively used for the j^{th} beat of type A or B (with j=1,2...,N/2) and the i^{th} sample point in a beat. Δ_A and Δ_B are correcting factors that keep track of the beat morphology evolution and limit the effect of any beat that might be affected by noise. The alternans estimate is finally determined as follows:

$$TWA_j = \max_{i=T_{onset}}^{i=T_{offset}} \left| A_j(i) - B_j(i) \right| \quad (4)$$

According to this technique, if N (N=128) ECG beats are considered, N/2 TWA values are computed. In the presence of stationary TWA, as the one simulated here, TWA_j assume a constant value, independently of j. Thus, for each tracing the MMAM provides the following quantitative estimation of TWA:

$$A_{MMAM} = TWA_j \quad \forall j \quad (5)$$

Adaptive-match-filter method (AMFM) [8]. TWA is, by definition, characterized by a specific frequency, f_{TWA}, given by half heart rate. To account for physiological variations of the RR interval, a narrow frequency band, instead of a single frequency, is assumed by this technique to characterize the TWA phenomenon. On this basis, the adaptive match filter (AMF) is implemented as a 6^{th} order bidirectional Butterworth pass-band filter having the passing band $2 \cdot df_{TWA}$=0.12 Hz wide and centered in f_{TWA}. In particular, the AMF consists of a cascade of a low pass filter (LPF) with cut-off frequency $f_{LPF} = f_{TWA} + df_{TWA}$, and a high pass filter (HPF) with a cut-off frequency $f_{HPF} = f_{TWA} - df_{TWA}$. The squared module of the AMF transfer function is as follows:

$$\begin{aligned} \left|H_{AMF}(\omega)\right|^2 &= \left|H_{LPF}(\omega)\right|^2 \cdot \left|H_{HPF}(\omega)\right|^2 = \\ &= \frac{1}{1+\left(\frac{\omega}{\omega_{LPF}}\right)^6} \cdot \frac{\left(\frac{\omega}{\omega_{HPF}}\right)^6}{1+\left(\frac{\omega}{\omega_{HPF}}\right)^6} \end{aligned} \quad (6)$$

where, $\omega_{LPF}=2\pi f_{LPF}$ $\omega_{HPF}=2\pi f_{HPF}$.

The input of the filter is the ECG signal, while the output is the TWA signal, a sinusoid characterized by constant phase and, possibly, amplitude modulation, with its maxima and minima occurring in correspondence of the T waves. A quantitative measure of TWA, A_{AMFM}, is thus provided by the sinusoid amplitude, which in the presence of stationary TWA, keeps constant.

2.4. Statistics

The ability of each method to quantify TWA was evaluated comparing the TWA quantitative outputs provided by each method when analyzing a synthetic ECG tracing with the simulated A_{MAX} and A_{MEAN}. In particular, two percentage errors were defined as follow:

$$\varepsilon_{MAX} = \left|A_m - A_{MAX}\right| / A_{MAX} \quad (7)$$

$$\varepsilon_{MEAN} = \left|A_m - A_{MEAN}\right| / A_{MEAN} \quad (8)$$

where m is either equal to FFTSM, MMAM, and AMFM.

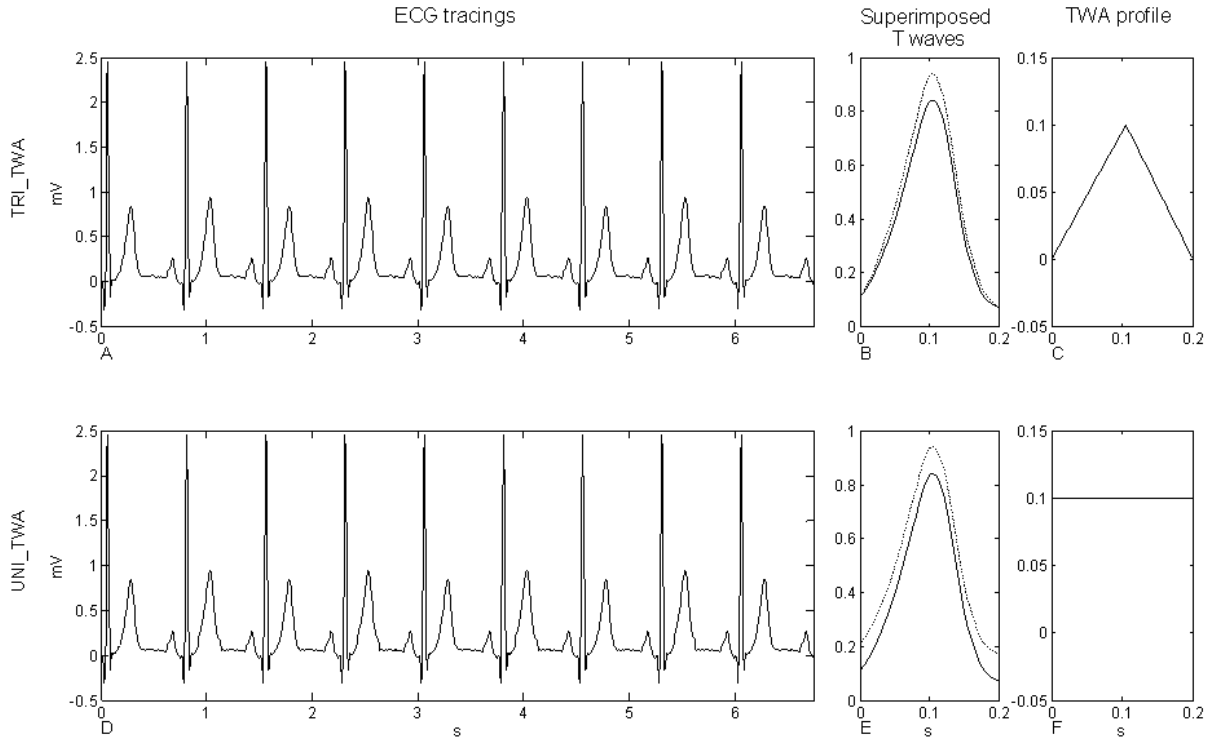

Figure 1: Graphical representation of the TRI_TWA and UNI_TWA synthetic ECG tracings (panels A and D), together with corresponding superimposition of two consecutive T waves (panels B and E) and TWA profiles (panels C and F).

3. Results

Application of the FFTSM, the MMAM, and the AMFM to TRI_TWA yielded 57 μV, 100 μV and 50 μV, TWA amplitude estimations, respectively. On the other hand, 100 μV TWA amplitude was provided by each method after their application to UNI_TWA (Table 1). Consequently, ε_{MAX} and ε_{MEAN} values provided by all methods were, in general, greater than zero only when analyzing TRI_TWA. In the specific, when assuming A_{MAX} as TWA quantitative definition, the FFTSM and the AMFM estimated TWA with a significant ε_{MAX} of 43% and 50%, respectively, whereas the MMAM estimated TWA with no error (Table 2). Instead, when assuming A_{MEAN} as TWA quantitative definition, the FFTSM and the MMAM estimated TWA with an ε_{MEAN} of 14% and 100%, whereas the AMFM estimated TWA with no error.

4. Discussion and conclusion

The present study demonstrates that the three different methods (FFTSM, MMAM, and AMFM) considered here provide different quantitative information of TWA. Indeed, in the absence of a standardized TWA parameterization, each TWA identification technique relies on its own quantitative definition of TWA.

Table 1: TWA measurements provided by the FFTSM, the MMAM, and the AMFM when analyzing TRI_TWA and UNI_TWA.

	TRI_TWA (μV)	UNI_TWA (μV)
FFTSM	57	100
MMAM	100	100
AMFM	50	100

Table 2: ε_{MAX} provided by the FFTSM, the MMAM, and the AMFM when estimating TWA from TRI_TWA and UNI_TWA.

	TRI_TWA	UNI_TWA
FFTSM	43%	0%
MMAM	0%	0%
AMFM	50%	0%

Table 3: ε_{MEAN} provided by the FFTSM, the MMAM, and the AMFM when estimating TWA from TRI_TWA and UNI_TWA.

	TRI_TWA	UNI_TWA
FFTSM	14%	0%
MMAM	100%	0%
AMFM	0%	0%

The choice of comparing the FFTSM [6], the MMAM [7], and the AMFM [8] is based on the fact that the former two are the only techniques implemented in commercial ECG machines (CH2000 and Heartwave, Cambridge Heart Inc, Bedford, MA; and CASE-8000, GE Medical Systems, Milwaukee, WI, respectively), whereas the latter is our own technique recently tested in both simulated and clinical settings [8, 10-12]. After having assumed two possible quantitative definitions of TWA, respectively designated as the maximum (A_{MAX}) and the mean (A_{MEAN}) values of the amplitude absolute difference between two consecutive T waves, two simulated ECG tracings with controlled values of A_{MAX} and A_{MEAN} were submitted to the three methods for TWA identification. In the specific, the synthetic ECG tracings were respectively affected by stationary TWA with a triangular profile (TRI_TWA), in which A_{MAX} was twice A_{MEAN} (A_{MAX}=100 μV and A_{MEAN}=50 μV), and a uniform profile (UNI_TWA), with equal A_{MAX} and A_{MEAN} (A_{MAX}= A_{MEAN}=100 μV). The values of the TWA estimates by the FFTSM, the MMAM and the AMFM were then compared to the simulated values of A_{MAX} and A_{MEAN}.

Our results show that, when analyzing UNI_TWA, all methods quantified TWA with no error, independently of TWA quantitative definition (Tables 1 to 3). Since in this case A_{MAX} equals A_{MEAN}, no further information about the kind of measure provided by each method can be inferred. More interestingly, when analyzing TRI_TWA, the FFTSM estimated TWA with an ε_{MAX} of 43% and an ε_{MEAN} of 14%. Thus, the TWA measure provided by this method was closer to A_{MEAN} than A_{MAX}. This result finds its rational in formula (2) of the FFTSM procedure, which provides an approximation (being the square root a nonlinear operator) of the mean amplitude alternation averaged over the T-wave width. The MMAM estimated TWA with an ε_{MAX} of 0% and an ε_{MEAN} of 100%. Consequently, as can also be deduced from formula (4), the MMAM quantifies TWA as the maximum amplitude distance between two consecutive T waves. Finally, the AMFM estimated TWA with an ε_{MAX} of 50% and an ε_{MEAN} of 0%, indicating that the amplitude of the TWA signal at the output of the match filter (equation (6)) is a direct measure of the mean TWA amplitude.

In conclusion, different TWA identification techniques rely on different quantitative definitions of TWA, and thus provide different characteristics of this phenomenon. In the specific, when considering the three methods analyzed here, it should be noticed that the FFTSM and the AMFM provide estimates of A_{MEAN}, whereas the MMAM provides an estimate of A_{MAX}.

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