Heart-Rate Adaptive Match Filter Based Procedure to Detect and Quantify T-Wave Alternans

L Burattini, R Burattini

Polytechnic University of Marche, Ancona, Italy

Abstract

Aim of the present study was to test our heart-rate adaptive match filter procedure for TWA analysis, which includes a) a heart-rate adaptive match filter, that filters out every ECG component but the TWA and quantifies TWA in terms of the duration (TWAD), amplitude (TWAA), and magnitude (TWAM, defined as TWAD × TWAA); and b) a statistical threshold criterion (STC) to identify, among all TWA detected cases, the ones (TWA+) most likely associated to an increased risk of sudden cardiac death. Our test, performed on the database assembled for the PhysioNet/Computers in Cardiology Challenge 2008, yielded the following results. On average, the data set was characterized by TWAD= 63±31 beats, TWAA= 48±77 μV, and TWAM= 3249±5107 beats μV. Based on our STC, TWA+ cases were 21, yielding a ranking score of 0.684. Use of STC, in the perspective of discriminating risky cases, among all detected TWA cases, might have limited our score.

1. Introduction

A century after it was first reported by Hearing [1], T-wave alternans (TWA) is widely recognized as an important, non-invasive indicator of risk of sudden cardiac death (SCD). During the last decades, several algorithms for detecting and quantifying TWA have been proposed. Still, their validation and/or comparison remains very difficult, because of the lack of generally accepted objective criteria for measuring TWA and specific validation data sets. To overcome these limitations, the Physionet/ Computers in Cardiology Challenge 2008 provided a data set consisting of 100 ECG recordings, most of which obtained from healthy subjects and cardiovascular patients. Aim of the present study was to test our heart-rate adaptive match filter procedure for TWA analysis, which includes: a) an adaptive match filter to quantify TWA in terms of the TWA duration, amplitude, and magnitude (this last one being defined as the product of the previous two); and b) a statistical threshold criterion to identify, among all TWA cases, the ones that are likely associated to an increased risk of SCD [2, 3].

A Challenge ranking score measured the agreement of our results with those obtained with different methods by the other Challenge participants.

2. Methods

Challenge data set. This database has been assembled for the PhysioNet/Computers in Cardiology Challenge 2008. It contains 100 multichannel ECG records (TWA00, TWA01, …TWA99) approximately two minutes long, sampled at 500 Hz, and with 16 bit resolution over a ± 32 mV range. This data set includes patients affected by myocardial infarction, ventricular tachyarrhythmias, transient ischemia, and other risk factors for SCD, as well as healthy control subjects and 32 synthetic cases with calibrated amounts of TWA. These last ones were realized with 6 model ECGs. TWA amplitude of 30 of them, obtained using models A to E are reported in Table 1; the remaining 2, obtained using model E, are identified as TWA52 and TWA81 and are known to have no TWA. In most cases, each record contains the standard 12 diagnostic ECG-signal leads, but a few contain only 2 (15 recordings) or 3 (13 recordings) leads. No specific information about individual records has been provided.

Table 1: Names (ID) and TWA amplitude (TWAA, in μV) of 30 synthetic ECGs obtained using models A to E.

A	B	C	D	E
ID (TWAA)	**ID (TWAA)**	**ID (TWAA)**	**ID (TWAA)**	**ID (TWAA)**
TWA34 (60)	TWA17 (13)	TWA01 (45)	TWA06 (17)	TWA13 (60)
TWA50 (15)	TWA29 (45)	TWA15 (15)	TWA09 (30)	TWA25 (4)
TWA51 (8)	TWA33 (10)	TWA28 (2)	TWA21 (10)	TWA35 (2)
TWA64 (4)	TWA78 (2)	TWA69 (4)	TWA30 (2)	TWA72 (17)
TWA76 (2)	TWA97 (17)	TWA88 (6)	TWA67 (6)	TWA73 (13)
TWA79 (30)	TWA98 (6)	TWA91 (60)	TWA70 (8)	TWA82 (8)

Adaptive match filter for TWA detection and parameterization. This procedure, recently assessed by ourselves [2, 3], makes use of a heart-rate adaptive match filter (AMF) to detect TWA by filtering out every ECG component (including noise and baseline wandering related ones) but the TWA. At a given hear rate, TWA is, by definition, characterized by a frequency f_{TWA}= 1/(2×RR) Hz, where RR is the RR interval (in sec). In physiological conditions, however, some RR variability may exists, so that a narrow frequency band, instead of a single frequency, characterizes TWA. On this basis, our AMF was designed as a 6th order, bidirectional Butterworth band-pass filter, with its passing band centred in f_{TWA} (passing band $2 \cdot df_{TWA}$, where df_{TWA}=0.06 Hz), and realized as a cascade of a low pass filter (LPF; cut-off frequency $f_{LPF}= f_{TWA}+ df_{TWA}$), and a high pass filter (HPF; cut-off frequency $f_{HPF}= f_{TWA}-df_{TWA}$). The squared module of the AMF transfer function is expressed by the following equation:

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

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

The input signal of our AMF is a rough ECG tracing, which is required to meet the following heart-rate stability requirement [2]:

$$SDRR < 0.1 \cdot MRR \quad (2)$$

where SDRR and MRR are, respectively, mean and standard deviation of RR intervals of an ECG tracing. This requirement is necessary to a) exclude cases in which TWA is driven by heart-rate (HR) variability [4], and b) allow TWA analysis of ECG recordings obtained in physiological conditions (in which some HR-variability occurs).

The output of our AMF is a TWA signal, which equals zero when TWA is not present, and shows a sinusoidal time course with constant phase and, possibly, amplitude-modulation, in the presence of TWA. The sinusoid amplitude, whose maxima and minima occur in correspondence to the T-waves, provides a local estimate of TWA amplitude (A_{TWA}; in μV) associated to each single beat. All local A_{TWA} values are used to compute global (i.e. relative to the ECG tracing) TWA parameters, such as TWA duration (TWAD, beats; defined as the total number of beats with alternating T-waves), TWA amplitude (TWAA, μV; defined as the mean A_{TWA} over all alternating T-waves), and TWA magnitude (TWAM, beat×μV; defined as the product of TWAA times TWAD). TWAD, TWAA and TWAM parameter values are determined in each lead. Corresponding values from the available leads (X,Y,Z) are then averaged for final TWA characterization relative to a specific ECG.

Criterion for risky TWA identification. Our statistical threshold criterion (STC) was introduced in a previous report [2] to discriminate risky (TWA+) from normal (TWA-) TWA. The TWA+ region, in the TWAD-TWAA plane, is defined by the following inequalities (Fig.1):

$$\text{TWAD} > \text{THRD} \quad \text{or} \quad \text{TWAA} > \text{THRA} \quad \text{or} \quad \text{TWAM} > \text{THRM} \quad (3)$$

where THRD=96 beats, THRA= 105 μV and THRM=5671 μV×beat. By definition, the threshold line identified by THRM in the TWAA-TWAD plane is a segment of hyperbola (Fig. 1). To gain further ability to discriminate among different risk levels, the TWA+ zone was divided into four sub-zones by drawing the boundary dashed lines relative to THRD and THRA threshold values (Fig. 1). These four TWA+ sub-zones were characterized by low duration and low amplitude (LDLA), low duration and high amplitude (LDHA), high duration and low amplitude (HDLA), and high duration and high amplitude (HDHA), respectively, according to the following inequalities:

$$\text{LDLA}: \begin{cases} \text{TWAD} \le \text{THRD} \\ \text{TWAA} \le \text{THRA} \\ \text{TWAM} > \text{THRM} \end{cases} \quad (4)$$

$$\text{HDLA}: \begin{cases} \text{TWAD} > \text{THRD} \\ \text{TWAA} \le \text{THRA} \end{cases} \quad (5)$$

$$\text{LDHA}: \begin{cases} \text{TWAD} \le \text{THRD} \\ \text{TWAA} > \text{THRA} \end{cases} \quad (6)$$

$$\text{HDHA}: \begin{cases} \text{TWAD} > \text{THRD} \\ \text{TWAA} > \text{THRA} \end{cases} \quad (7)$$

Challenge ranking score. A ranking score has been associated to our entry form, containing TWAA estimates. Only TWA cases satisfying the STC, but not necessarily the heart-rate statistical requirement, have been reported in the entry form as showing TWAA>0. Each record received a median ranking (the median of the ranks assigned to it by the entries) and a reference

ranking (made by sorting the median ranks). A score for the entry was computed as the Kendall rank correlation coefficient between the entry ranking and the reference ranking, where 1 is perfect agreement and -1 is perfect disagreement (see Challenge rules for details).

3. Results

In 11 ECG recordings (namely, TWA01, TWA05, TWA16, TWA17, TWA28, TWA32, TWA46, TWA69, TWA74, TWA78, and TWA90), HR-variability did not satisfy our heart-rate stability requirement.

The TWA and HR characteristics of the remaining 89 ECG recordings are summarized in Table 2. Among these, 21 were recognized as TWA+ by our STC (Table 2, Fig. 1), 4 following in LDLA (TWA22, TWA26, TWA58, TWA95), 9 in HDLA (TWA06, TWA09, TWA13, TWA29, TWA34, TWA59, TWA79, TWA91, TWA97), 7 in LDHA (TWA02, TWA07, TWA44, TWA57, TWA68, TWA80, TWA84), and 1 in HDHA (TWA37).

When comparing TWA- cases against TWA+ cases, we observed that the ones falling in the LDLA and HDHA zones had significantly higher TWAD, TWAD and TWAM. Instead, those in the LDHA zone had significantly higher TWAA and TWAM, whereas those in the HDLA had significantly higher TWAD (Table 3).

TWA cases with known TWA are also represented in Fig.1 . Eight of them fell in the LDHA region, whereas the others, although showing TWA, fell in the TWA- region (i.e. their TWA level was not considered risky).

Our ranking score, yielded by the TWA+ cases, was 0.684.

Table 2. TWA (TWAD, TWAA, and TWAM) and HR characteristics of the 89 ECG recordings satisfying the HR-stability requirement. Values are expressed in mean±sd.

	ECGs (n=89)
TWAD (beats)	63±31
TWAA (μV)	48±77
TWAM (beats μV)	3249±5107

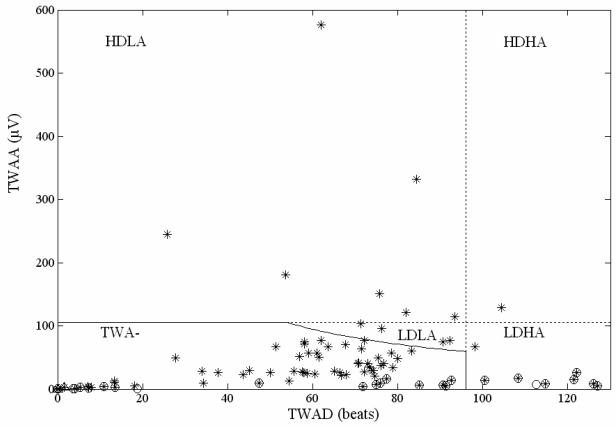

Figure 1. TWA cases as measured by our AMF procedure (*), with known amount of TWA (o), and with known absence of TWA (Δ). According to our STC, normal TWA cases fall in the TWA- region, whereas abnormal (TWA+) cases fall in one of the TWA+ zones identified as LDLA, HDLA, LDHA, HDHA.

Table 3. TWA (TWAD, TWAA, and TWAM) and HR characteristics of the normal (TWA-) and abnormal (LDLA, HDLA, LDHA, HDHA) cases of TWA. Values are expressed in mean ± sd.

	TWA- (n=68)	LDLA (n=4)	HDLA (n=9)	LDHA (n=7)	HDHA (n=1)
TWAD (beats)	54±26	83±10*	115±11*	68±23	104±0*
TWAA (μV)	29±23	88±14*	19±19	246±165*	129±0*
TWAM (beats·μV)	1795±1520	6857±491*	2168±1830	15207±11515*	13743±0*

*cases for which comparison with TWA- corresponding parameter was characterized by $p<0.05$ (Wilcoxon rank sum test)

4. Discussion and conclusions

ECG-TWA is generally recognized as a marker for an increased risk of malignant arrhythmias, and several methods, including our own [2,3], have been reported for its detection and characterization. The Computers in Cardiology Challenge 2008 is an important event for scientific evaluation and comparison of these techniques, by providing a specific evaluation ECG data set.

We participated to the Challenge by analyzing TWA with our procedure which mainly consists of TWA quantification (by means of our AMF), and TWA identification (by means of our STC).

TWA is well known to be more evident in the

presence of fast heart rates (> 100 beats/min), usually reached through pacing, exercise, and drugs [5]. Such treatments have the additional advantage to keep heart-rate essentially constant, so that cases of TWA driven by heart-rate variability [4] are avoided. Still, they have the major limitation not to be applicable to most routine ECG testing, during which identification of subjects at increased risk of SCD is desirable. Consequently, the Challenge data set enrolled ECG recordings showing a large variety of physiological hart rates (43-132 beats/min), which, in the absence of further information, are assumed to be spontaneously reached. Eleven of these recordings, however, did not show stable heart rate and, consequently, were rejected by our procedure because not satisfying the heart-rate stability requirement (Eq. 2).

Our AMF for TWA quantification is a time domain technique that has the advantage to be directly applied to the row ECG recording, without any pre-processing for noise, artefacts, or baseline removal. Only detection of the R peaks is required. No assumptions on TWA stationarity, minimal TWAD or minimal TWAA are made, so that both sustained (long TWAD) and transient (short TWAD) cases of TWA are detected and properly characterized. Since the AMF provides a set of TWA parameters (TWAD, TWAA, and TWAM) for each available lead, in the absence of specific directives, these sets were averaged over the leads for a final TWA characterization of an ECG record [2].

Not having information about which tracings of the data set belonged to healthy individuals, we used a STC defined in a previous study [2] on a population of 200 healthy subjects, who, according to clinical believes, should not show risky TWA. The STC identifies a normality (TWA-) region in the TWAD-TWAA plane, out of which risky (TWA+) cases of TWA fall. For a better characterization of the TWA+ cases, the TWA+ region is divided into 4 subzones: HDLA and HDHA, where sustained TWA cases, with respectively low and high amplitude, fall; LDHA, where transient TWA cases fall; and LDLA, where intermediate cases of TWA fall. This further classification of the TWA+ cases will be a useful tool for future follow-up studies finalized to identify which kind of TWA (sustained or transient, high or low amplitude) is more associated to the risk of ventricular arrhythmias and SCD. Threshold values (THRD=96 beats, THRA=105 μV and THRM=5671 μV×beat) delimiting the various regions were obtained for 3-lead, 128-beat ECG tracings, and are optimal only for ECG recordings of that kind. Even though only some tracings in the Challenge data set were 3-leads, 128-beats ones, the STC has been applied to all of them.

Our final ranking score was 0.684. Considering that such score was obtained after submitting only cases that satisfied the STC, and that information on the synthetic ECG tracings were given only after the entry form submission, such score supports the ability of our technique to detect and quantify TWA.

Our AMF and STC provide a TWA characterization that depends of the ECG length and the number of leads. For ECG recordings with variable length and number of leads, as those in the data set, the threshold values of the STC should be adjusted. Adjustment was not possible in this study, since no information was provided as to which recordings enclosed in the data set belonged to healthy subjects. In addition, TWA quantification of a single tracing was arbitrary, since it was not clear if a single lead, or a combination of leads, should have been considered when quantifying TWA.

In conclusion, this Challenge has focused the attention on TWA as a promising, non-invasive indicator of the risk of SCD. The need of standards in the TWA analysis process was highlighted. Our procedure appears a suitable tool to provide such standards. It provides a TWA characterization both in time and amplitude, thus distinguishing transient from sustained TWA. Involvement of an STC, is important in the perspective of discriminating, among all TWA detected cases, the ones (TWA+) that are at increased risk of SCD.

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Address for correspondence

Prof. Roberto Burattini, Dr. Eng.
Department of Biomedical, Electronics and Telecommunication Engineering
Polytechnic University of Marche
60131 Ancona, Italy
E-mail address: r.burattini@univpm.it