T-Wave Alternans Ranking: Striking Disagreement between Two Vectorcardiographic Measures of Repolarization Heterogeneity

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Abstract

In an attempt to study the importance of T-wave feature selection for T-wave alternans (TWA) analysis, we compared the alternans in two vectorcardiographic variables: maximal T-loop vector (MaxT) and the T-loop vector integral (Ti). We analyzed TWA in the 72 standard 12-lead ECGs comprised in the Physionet TWA Challenge Database with our research ECG/VCG processing program LEADS. We computed TWA by taking the absolute differences of the even and odd averaged beat values of Ti and MaxT (MaxT-TWA and Ti-TWA); also percentual alternans (%MaxT-TWA and %Ti-TWA) was computed. Finally, we computed both the Pearson and Kendall tau-b correlation coefficients between the MaxT-TWA and Ti-TWA, and between %MaxT-TWA and %Ti-TWA. All correlation coefficients differed significantly ($P<0.01$) from zero, but were relatively low ($R=0.333$-0.663). We conclude that T-wave features contain only in part common information; the selection of the T-wave feature in which TWA is computed deserves more attention.

1. Introduction

Since the first report of (visible) T-wave alternans (TWA) by Hering in 1908 [1], this phenomenon was observed in various patient populations [2-5]. It became apparent that visible TWA was a harbinger of serious arrhythmias [2]. Adam et al. found that invisible microvolt TWA in patients was related to visible TWA, and thus a promising tool for identifying high risk patients for ventricular arrhythmias [6]. Subsequently, multiple clinical/experimental studies confirmed the relevance of microvolt TWA as a marker of vulnerability to ventricular arrhythmias [6-12].

The electrocardiographic phenomenon of TWA is caused by alternans in cellular repolarization properties, where lower alternans amplitudes may be caused by generalized fluctuations in the heart, while larger alternans amplitudes are possibly caused by increased and alternating contrasts in regional (e.g., apical-basal) repolarization properties [13].

In developing microvolt TWA analysis algorithms, much attention has been spent to the methods needed to reliably extract the every-other-beat alternation in the selected T-wave feature amidst fluctuations with other periodicity and amidst noise. Amongst others, spectral methods, complex demodulation, correlation, Karhunen-Loève transform, Capon filtering, periodicity transform, statistical tests, moving average, and Laplacian Likelihood Ratio methods are used [14].

Relatively less research was done to the T-wave feature in which the alternans should be measured. In most studies, the utilized T-wave feature (e.g., normalized aggregated TWA energy per sample [15], (un)normalized aggregated T-wave amplitude difference per sample [11,16], the T-wave area alternans per 10 ms bin [17], and the maximal absolute difference within the ST-T region [18]) is presented without explicit motivation. Such motivation could be found in the linkage of the T-wave feature to the underlying repolarization alternans phenomenon at the cellular level.

We hypothesized that the selection of a T-wave feature is essential for the relative position of a given subject when ECGs of a group of persons are ranked according to their TWA magnitude. When this view is correct, the selected T-wave feature is essential for the value of TWA analysis for individual risk assessment. To address our hypothesis, we compared the alternans in the T-loop vector integral and in the maximal T-loop vector magnitude. Computer simulations and animal studies have shown that these vectorcardiographic variables are indexes for repolarization heterogeneity [19,20].

2. Methods

2.1. Study population

We analyzed the 72 standard 12-lead ECGs in the PhysioNet/Computers in Cardiology Challenge 2008 database (the remaining 28 recordings had 2 or 3

unspecified leads only, which rendered them unsuitable for vectorcardiographic analysis). The 72 ECGs recordings were sampled at 500 Hz and had a 16 bit resolution over a ± 32 mV range. The ECGs were recorded from patients with transient ischemia, ventricular tachyarrhythmias, myocardial infarctions, and other risk factors for sudden cardiac death, as well as in healthy controls. Also, synthetic cases were added with calibrated amounts of T-wave alternans. Whether or not the ECG was real or synthesized and what was the individual diagnosis was blinded. Each record was approximately two minutes in duration.

2.2. ECG processing

We analyzed the first 30 seconds of each ECG recordings with our research ECG/VCG processing program LEADS (Leiden ECG Analysis & Decomposition Software) [21]. Based on morphology comparison, interval criteria and noise estimation techniques, LEADS makes a selection of beats for subsequent averaging, rejecting beats of ectopic origin and rejecting noise beats. For the purpose of TWA analysis, LEADS processed all recordings twice (first the odd beats and then the even beats in the selection, see Figures 1 and 2).

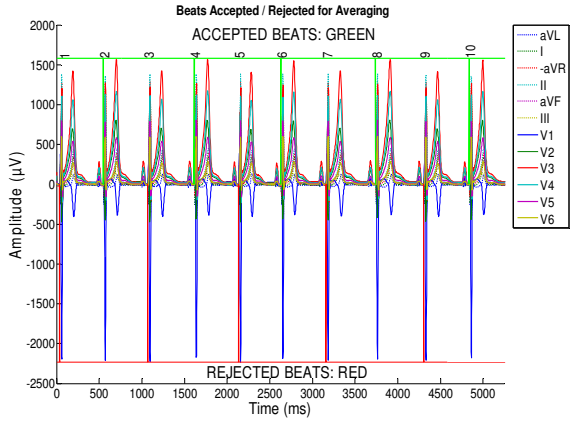

Figure 1. Beat selection (subject #34). Here, even beats are selected (**green**) and odd beats are rejected (**red**) for subsequent averaging.

After averaging, LEADS synthesizes, from the averaged beat (Figure 2), a vectorcardiogram (VCG, Figures 3 and 4) by applying the inverse Dower matrix [22]. LEADS computes multiple variables in the averaged beat, among which are the T-loop vector integral (Ti, in mV•ms) and the maximal T-loop vector magnitude (MaxT, in µV). For each ECG, the absolute differences between the "odd" and "even" values of Ti and of MaxT were taken as Ti-TWA and as MaxT-TWA, respectively. We also computed the percentual alternans, %Ti-TWA and %MaxT-TWA, by dividing Ti-TWA and MaxT-TWA by the average of the T-loop vector integral, and by the average of the maximal T-loop vector of the even and odd beats, respectively.

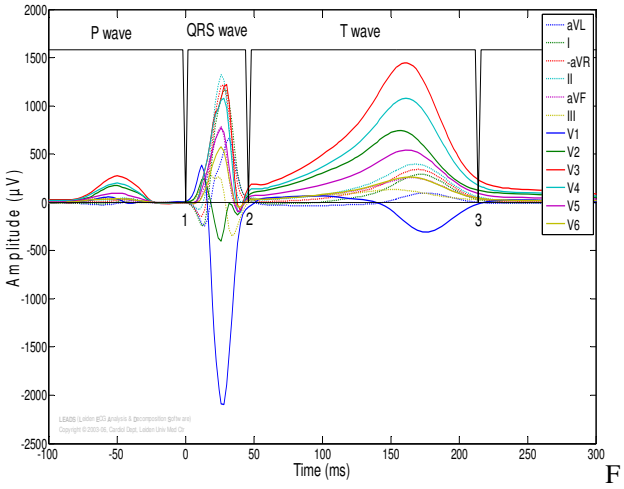

Figure 2. Averaged even beat (subject #34) with automatically determined landmarks in time (1: onset QRS, 2: J point (QRS offset), and 3: T offset).

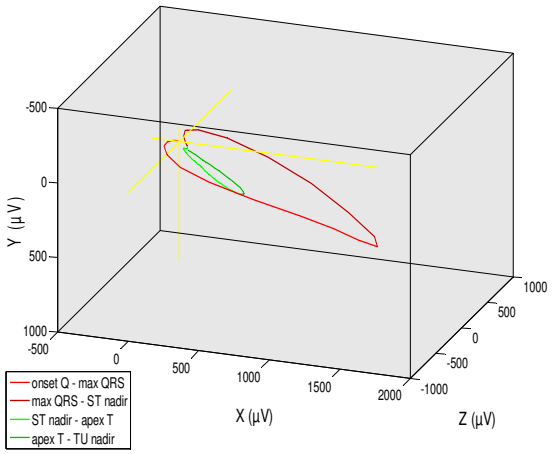

Figure 3. Vectorcardiogram of the even averaged beat of subject #34. **Red**: QRS-loop; **green**: T-loop.

2.3. Statistics

Statistical analysis was done with the Statistical Package for the Social Sciences Program (SPSS version 14.0, Chicago, Illinois). Data were expressed as mean ± SD and range. Both Pearson and Kendall tau-b correlation coefficients were computed between Ti-TWA

and MaxT-TWA and between %Ti-TWA and %MaxT-TWA. P-values <0.05 were considered significant.

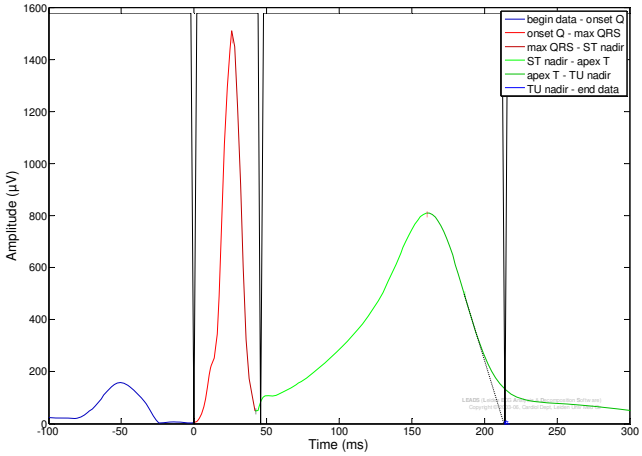

Figure 4. Vector magnitude of the even averaged beat of subject #34 with onset/offset QRS and offset T.

3. Results

All 72 ECGs were successfully processed by LEADS. The descriptive statistics of MaxT-TWA, Ti-TWA, %MaxT-TWA and %Ti-TWA are given in Table 1.

Pearson's correlation coefficients between MaxT-TWA and Ti-TWA (Figure 5) and between %MaxT-TWA and %Ti-TWA (Figure 6) were 0.634 and 0.663, respectively. Both correlations differed significantly (P<0.01) from zero.

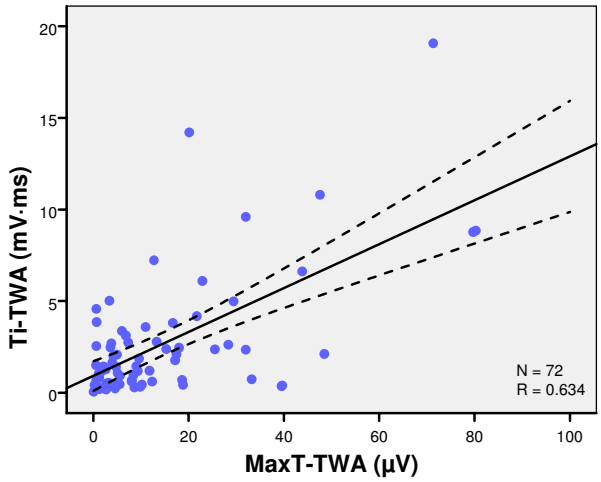

Figure 5. Scatterplot of Ti-TWA and MaxT-TWA. Continuous and dashed lines: linear least-squares regression line with 95% confidence intervals. R= Pearson's correlation coefficient.

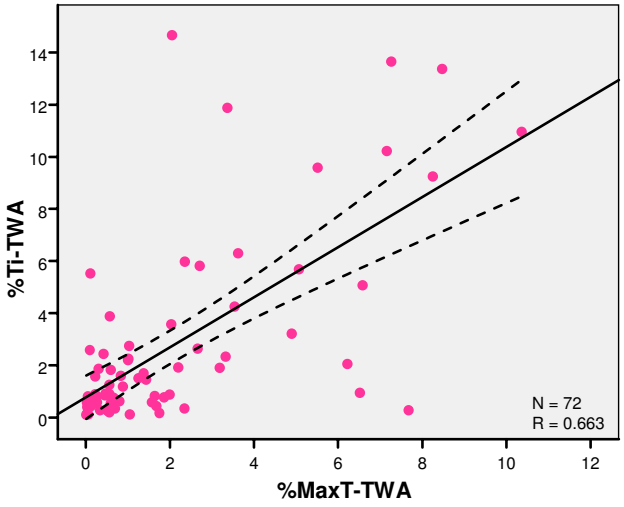

Figure 6. Scatterplot of %Ti-TWA and %MaxT-TWA. See also legend of Figure 4.

Variable	*Mean*	*SD*	*Min*	*Max*
MaxT-TWA (µV)	14.73	17.94	0.07	80.25
Ti-TWA (mV·ms)	1.95	2.77	0.04	16.26
%MaxT-TWA	2.08	2.48	0.01	10.36
%Ti-TWA	2.77	3.59	0.11	14.66

Table 1. Descriptive statistics of the TWA variables.

The Kendall tau-b correlation coefficients between MaxT-TWA and Ti-TWA and between %MaxT-TWA and %Ti-TWA were 0.333 and 0.422, respectively. Both correlations differed significantly (P<0.01) from zero.

4. Discussion & conclusion

In our study, we demonstrated that two T-wave features related to heterogeneity of the repolarization, yield TWA results that are significantly linearly related. However, the correlation coefficients are relatively low: only less that half of the variance in one variable can be explained by the other variable.

It can be seen in Figures 5 and 6 that a relatively large part of the subjects in this database has TWA values that are small and not too much different from each other. This means that the ranking order in this population will be extremely sensitive for small measurement errors. This explains why the Kendall tau-b correlation coefficients are much lower than the Pearson correlation coefficients. It is, therefore, possibly not reasonable to draw conclusions as to differences in ranking in this study population.

It appears from our data that even when the linear correlation coefficients are taken, the correlations between MaxT-TWA and Ti-TWA and between %MaxT-TWA and %Ti-TWA are significant, but relatively low, and less than half of the variability in one variable is explained by the variability in the other variable. Obviously, these variables yield strongly different TWA assessments, and this must have considerable impact on the predictive value of these variables in a clinical population at risk. Either the statistical performance of one variable will be much lower than the other, or the variables may have comparable performance but identify another type of high-risk patient. As our data show, TWA normalization (computation of percentual TWA) does not help to resolve this issue.

In conclusion, T-wave features contain only in part common information; the selection of the T-wave feature in which TWA is computed deserves more attention.

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