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New Approaches to T-wave Analysis from Surface ECG

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The most common method of assessing the ventricular repolarisation heterogeneity has been the QT dispersion (QTd). Although QTd was shown to be associated with heterogeneity, it does not provide a full picture and suffers from some technical drawbacks, mainly the T-end detection. Several new methods have been proposed as an alternative and/or a supplement to QTd. These make use of the amplitude of and area under the T wave, beat-to-beat morphology variation, morphological complexity of the T wave and the behaviour of the ECG vector. This article deals with a short review of such new methods proposed mainly since 1997 and attempts to provide the reader with an insight.

Introduction

The evidence that an increased heterogeneity of the ventricular repolarisation is closely associated with malignant ventricular arrhythmias, urged researchers to find quantitative ways to assess this heterogeneity. QT dispersion (QTd), which is defined as the maximum difference between QT intervals measured from different leads in 12-lead ECG, has become the most popular method. There are several studies in the literature on the cellular basis [1], the clinical utility [2] and the methodology [3] of QTd. Despite its popularity, which is mainly due to QTd's simplicity and intuitive nature, its poor reproducibility, which is mainly due to unreliable T-offset detection, raised questions about its applicability. Such concerns lead researchers to study the morphology of T wave. Cardiologists have already been using the morphological qualities of the T wave, however these are qualitative descriptions [4].

This review focuses on recent research on quantitative T wave morphology parameters. These new methods are aimed to be more reproducible than the time domain interval measurements (like QTd) and to provide information about the heterogeneity of ventricular repolarisation additional to QT interval related parameters, if not an alternative to them.

The Repolarisation Parameters

The new repolarisation parameters can be classified into four groups: (i) the amplitude related parameters; (ii) the frequency related parameters; (iii) the parameters based on decompositions; (iv) the vector based parameters.

The amplitude related parameters

The most intuitive way to describe the T wave morphology quantitatively is to use its amplitude and/or to use the area under it because it is easy to establish a relation between the heuristic methods of cardiologists and such parameters.

In a recent paper, Zareba et al. defined a set of parameters derived from the amplitude and the area of the repolarisation waves, i.e., the TU waves [5]. They calculated the following parameters from the median beats obtained from standard 12-lead ECG recordings of 34 affected LQTS patients (with QTc interval > 0.47 sec.) and 22 unaffected family members (with QTc interval <0.42 sec.): T_{amp} (maximum T wave amplitude), A_{tot} (total absolute area during JP segment), t_{A97} (time interval to accumulate 97% of A_{tot}), t_{A50} (time interval to accumulate 50% of A_{tot}), $t_{A25\text{-}75}$ (time interval to accumulate the mid 50% of A_{tot}), Pt_{A50} ($[t_{A50}/ t_{A97}] \times 100$), $Pt_{A25\text{-}75}$ ($[t_{A25\text{-}75} / t_{A97}] \times 100$). They used both the mean and the standard deviation (SD) of these parameters across 12 leads. Neither mean nor SD of T_{amp} and A_{tot} showed a significant difference between the two groups, whereas t_{A50}-SD and $t_{A25\text{-}75}$-SD provided the best discrimination of two groups, with a sensitivity (specificity) of 76% (75%) and 68% (70%) respectively. The mean value of Pt_{A50} also showed a significant difference between normals and LQTS patients (46 ± 5 vs 60 ± 10), which suggests a more asymmetric pattern in LQTS patients.

Yang et al. defined two new repolarisation parameters to characterise the rate of repolarisation, the maximum absolute slopes of the ascending and descending limbs of T wave (P_a and P_d) [6]. They investigated the relation between these parameters and the repolarisation duration parameters, like QT interval, in 562 normal subjects. All parameters were measured on lead V5 only. The new parameters had low correlation with the duration parameters ($|r| \leq 0.30$) but high correlation with the T wave amplitude ($|r| \geq 0.91$) and they exhibited disparity between sexes.

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The frequency related parameters

Apart from the parameters that describe T wave morphology, periodicity of the changes in the T wave morphology was also shown to have a consistent relationship with ventricular arrhythmias. Such behaviour is called T wave alternans (TWA), which is defined as a consistent beat-to-beat variation of the T wave morphology and/or polarity on an alternate beat basis during sinus rhythm. Much effort has been paid to detect such a variation. In a recent review paper, Murda'h et al. gives a background of TWA and lists the major methods of TWA detection [7]: Detection by visual inspection, the FFT based spectral analysis, the complex demodulation method.

Burattini et al. proposed a time-domain correlation index (ACI) to detect non-stationary T-wave alternans using T waves simulated by a sinusoid with changing amplitude [8]. ACI is defined for each T wave as its correlation with the median T wave and TWA is detected via the beat-to-beat variation of ACI. Hohnloser et al., on the other hand, used the spectral analysis method to show high correlation between TWA measured during exercise and atrial pacing [9]. This result suggests the use of TWA as a morphology parameter under crude conditions, like exercise testing. However, the number of technical requirements that has to be met, limits its use.

Narayan and Smith studied the temporal distribution of TWA during repolarisation [10]. They calculated a separate power spectral density (PSD_i) for each sampling instant (i) throughout repolarisation (R_{JT}: data window from J point to T offset) across 64 time-aligned T waves. The summation of PSD_i's was defined as the overall PSD representing the JT segment (or any subsegment as required). They calculated the magnitude of TWA for each time instant (TWA(i)) from the corresponding PSD_i (the peak at 0.5 cpb). A parameter of temporal distribution of TWA (T) was defined as the centre of mass of the area under TWA(i). They used the parameter T and PSD's corresponding to different segments of repolarisation to show that TWA is distributed later within repolarisation in patients with ventricular tachycardia. This result, together with Nearing et al.'s [11] somewhat contradictory results in favour of TWA distributed early within repolarisation, clearly show the importance of the intra-beat temporal variation of the T wave morphology, as well its spatial variation.

Steinbigler et al. extended the concept of TWA to variations at all periodicities (not only on an alternate beat basis as in TWA) by defining T Wave Spectral Variance (TWSV) [12]. They computed the two dimensional PSD of 1024 time-aligned T waves using FFT. The T waves were represented in a 2D matrix, the first dimension corresponding to time span of T waves and the second dimension corresponding to the sequence of consecutive T waves. Thus the resultant 2D PSD represents the frequency content of T waves in the first dimension in Hertz (Hz) and the beat-to-beat variation in the second dimension in cycles per beat (cpb). They defined TWSV Index (TWSV-I) as

$$\text{TWSV-I} = \frac{\text{Total energy in } (f1 < 50Hz \text{ AND} | f2 | > 0\ cpb}{\text{Total energy in } (f1 < 50Hz)}$$

Assuming that all T wave components are confined to the frequency band 0-50Hz, TWSV-I represents the inter-beat T wave morphology variation as a percentage of total T wave variation. They managed to identify the patients with ventricular arrhythmias in a population of 200 post-MI patients, with 89% sensitivity and 78% specificity.

Couderc et al. demonstrated the use of Wavelet Transformation (WT) in detecting abnormal ventricular repolarisation patterns in a population of 43 LQTS patients and 29 normal subjects [13]. They applied WT to the median beats of 10 sec. segment of each lead separately. The WT coefficients of the two groups were compared at every time and frequency (scale) point in the time-frequency plane. They selected the wavelets associated with a significant separation (p-value < 0.0001) and defined the sum of their coefficients as a single T wave parameter. The ROC area was 96% for the WT coefficients in lead I while it was 88% for the QTc interval.

The parameters based on decompositions

The methods described in this section represent the T waves in terms of some mathematically defined functions (waveforms) which are either derived from the T wave itself or are defined independently. In the following, these functions are named as basis functions in general, although this term is not correct for all.

Padrini et al. modelled the T and U waves as a superposition of the action potentials (AP) of a set of cells [14]. After some justified simplifications, they decomposed TU waves as follows: $TU(t) = S1(t) - S2(t) + L1(t) - L2(t)$. The basis functions S1 and S2, model the T wave whereas L1 and L2 model the U wave. The Hill's function ($A(t) = A_{inf} \times t^n/[T_{50}^n + t^n]$) was used to generate these basis functions. The model parameters (A_{inf}, T_{50}, n) for each function are determined by using a supervised best-fitting procedure. They showed that various TU wave morphologies can be described with this model and that the accuracy of the model is independent of the complexity of the TU wave. This model provides a separate description of the T and U waves, six parameters for each.

Priori et al. applied the Principal Component Analysis (PCA) to the ST-T segment of 12-lead Holter ECG recordings to quantify the complexity of repolarisation in 40 healthy subjects (QTc: 414 ± 18 ms.) and 36 LQTS patients (514 ± 59 ms.) [15]. They defined the ST-T segment as starting from the QRS offset and ending at a point determined according to the Bazett's formula, thus avoided the accurate time domain detection prob-

lem. Three parameters were defined using the singular values ($\sigma_1 \geq \sigma_2 \geq \ldots \geq \sigma_8 \geq 0$) that represent the relative magnitudes of the principal orthogonal components (basis functions) of the repolarisation pattern:

$$CR = (\sigma_2 / \sigma_1) \times 100$$
$$CR1 = \left(\sigma_2 / \sqrt{\sigma_1^2 + \Lambda + \sigma_8^2} \right) \times 100$$
$$CR2 = \left(\sqrt{\sigma_2^2 + \Lambda + \sigma_8^2} / \sqrt{\sigma_1^2 + \Lambda + \sigma_8^2} \right) \times 100.$$

Each parameter above is a measure of the dimensionality of the repolarisation. In case of identical repolarisation patterns in all channels, all of them would be zero. They computed CR for four consecutive beats and used their average. CR_{24h}, which is defined as the average of hourly CRs over 24 hours, had sensitivity and negative predictive value identical to that of QTc, 88% and 91% respectively and no significant correlation with therapy, symptoms and diagnostic score. On the other hand, a single CR measurement had a very poor diagnostic power due to the increased variability of CR over 24 hours in LQTS patients.

A similar method, the Karhunen-Loeve Transform (KLT), was applied to the ST-T segment by Laguna et al. [16]. They computed a set of basis functions (eigenvectors that represent the principal waveform patterns) using a set of beats, the training set, and used the most significant two of these functions throughout the rest of the analysis, unlike the PCA analysis described above where there was no fixed basis. They used the time series of the corresponding coefficients (λ_1, λ_2) for ischaemia detection. λ_1 and λ_2 are analogous to σ_1 and σ_2 in PCA analysis. 65% sensitivity and 54% specificity was achieved in the ESC ST-T database.

The vector-based parameters

The problems associated with the scalar measurements and the fact that the propagating action potentials have both a direction and a magnitude led the researchers to work on vector-based parameters.

Badilini et al. used the three-dimensional (3D) loop that the 3D ECG vector, **m**, traverses during T wave to assess the ventricular repolarisation heterogeneity in a population of 25 normals, 30 post-MI patients and 17 LQTS patients [17]. They computed the normalised eigen-values associated with the three principal components (λ_{1n}, λ_{2n}, λ_{3n}) and defined the following parameters:

$$RP = \sqrt{\gamma_{2n} / \gamma_{1n}}$$
$$\Delta Q = [\max(m_3) - \max(m_3)] \Big/ \sum_{i=1}^{3} \lambda_i \qquad \mathbf{m} = [m_1\, m_2\, m_3]$$
$$AVQ = [\text{mean}(m_3)] \Big/ \sum_{i=1}^{3} \lambda_i$$

RP describes the roundness of the T loop and is analogous to previously defined CR parameter [15]. It increases with increasing roundness. The other parameters, together with λ_{3n}, describe the planarity (confinement of the loop to a 2D space which is a plane) of the loop by assessing the component of the loop in the 3rd dimension. They all increase with decreasing planarity. Their results can be summarised as follows: (i) λ_{1n}, λ_{2n} and RP can discriminate between the normals and the post-MI group but not the LQTS group (increased roundness of the loop in post-MI group). (ii) ΔQ and AVQ can discriminate between the normals and the LQTS group but not the post-MI group (decreased planarity in LQTS group). (iii) λ_{1n}, λ_{2n}, RP and AVQ can discriminate between the post-MI group and the LQTS group (decreased roundness and planarity in LQTS group). They also calculated the QTd and the standard deviation of QT intervals (SDQT) and showed that although these parameters could separate normals from LQTS and post-MI patients, they were unable to discriminate between the LQTS patients and the post-MI patients.

Kors et al. showed an association between the orientation of the 3D mean ECG vector (leads X, Y, Z) during ventricular repolarisation and fatal and non-fatal cardiac events in elderly people [18]. They defined a parameter as the angle between the x-axis and the 2D projection of the 3D mean vector onto XY plane. They defined the ranges for the normal, borderline and abnormal T axis as 15°:75°, −15°:15° and 75°:105°, −180°:−15° and 105°:180° respectively. The new parameter had a strong association with the conventional parameters, like QTd, ST depression, T wave inversion, etc. However, the T axis parameter proved to be associated with high risk of cardiac death in a multi-variate analysis and thus was suggested as an independent variable. In another study, they investigated the predictive value of an abnormal T-loop morphology (constructed from leads X, Y and Z) [19]. The T-loop morphology was classified as normal, borderline or abnormal based on the following loop parameters: (i) maximal spatial amplitude; (ii) width and sense of inscription of the T-loop in the horizontal plane; (iii) direction of the mean T-axis in the horizontal and vertical planes; (iv) direction and magnitude of the J-point displacement in the two planes. Both the T-loop classification and the T-axis parameter on its own proved to be associated with higher risks of cardiac death than any other risk indicator, including ST depression and T wave inversion. However, the T-loop proved to be only slightly better in predicting cardiac deaths.

Hurst reviews the Grant method of ST segment and T wave interpretation [20]. In this method, an ECG vector is constructed using standard 12-lead ECG signals. Hurst emphasises the locked-in relation between the QRS complex and the T wave. An abnormal depolarisation predetermines an abnormal repolarisation, so an abnormal T wave preceded by an abnormal QRS complex should be interpreted as normal. This relation is assessed by the relative orientations of the QRS and

the T vectors. The method also uses the absolute directions of these vectors in 3D physical space (the body).

Recently, Acar et al. introduced a set of new T wave morphology descriptors based on 3D ECG vectors, **s**, constructed from standard 12-lead ECG signals to describe the spatial, temporal and wavefront characteristics of the T wave [21]. **s** is defined as the projection of the 12-lead ECG onto the 3D space (S) defined by the most significant three principal components of the 12-lead ECG. **s** is analogous to **m** in Badilini's work. Acar et al. used the QRS complex and the T wave loops traversed by **s** in S and the transformation coefficients between S and the 12-lead ECGs to define the following descriptors:

- TMD (T wave Morphology Dispersion) introduces the concept of the spatial variation of the T wave morphology. It is defined as the average angle between the projections of the leads I, II, V2 to V6 in S. TMD decreases as the T wave morphologies of different leads get closer.
- TCRT (Total_Cosine_R_to_T) utilizes the concept of comparing the QRS complex and the T wave. It describes the relative orientation of the QRS and the T loops in S. The two loops were observed to deviate from each other in abnormal ECGs (TCRT < 0) and vice versa in normal ECGs (TCRT > 0).
- PL and PO are defined as the inner and outer areas of the T loop. The length of the T loop (LD) is also defined as a separate descriptor. They describe the temporal variation of the T wave by assessing the smoothness of the T loop. PL (PO) is high (low) for a smooth T loop (normal ECGs) and low (high) for irregular T loops (abnormal ECGs). On the other hand, LD was observed to decrease in abnormal ECGs.

TMD and TCRT were shown to be able to separate normals from HCM patients with higher sensitivity and specificity than the conventional parameters (ROC areas: QTd: 80.6%; QTc interval: 85.6%; TMD: 90.1%; TCRT: 90.9%). They also have better short-term reproducibility than the conventional parameters.

Discussion and Conclusion

QT dispersion, that has been used to describe the ventricular repolarisation heterogeneity, assesses only the time domain heterogeneity. However, repolarisation or any other cardiac process is a result of action potentials (APs) propagating in 3D space. Any abnormality of the conducting media (the heart) would cause changes in the propagation pathways as well as the time intervals. However, the changes in the pathways would affect the surface ECG morphologies but not necessarily the time intervals. So, QT dispersion is a measure of heterogeneity but fails to give the whole picture. The above described new repolarisation parameters emerged from this point and the need to avoid the well-known technical problems associated with the time domain measurements.

Zareba et al. did not provide any reproducibility analysis of their T wave area and amplitude related parameters [5]. Although these parameters do not require accurate time domain interval measurements, they unavoidably depend on the limits of the JP segment, which was defined as: JP_interval = QRS_offset + Median RR_interval − QRS_duration − PR_duration. On the other hand, since Yang et al.'s study is limited to normal subjects, the significance of the new maximum slope parameters in separating abnormal T waves is unknown [6]. They are likely to miss a simultaneous change in T wave amplitude and duration. The ratio of P_a and P_d can be used to describe the symmetry of T wave as a separate descriptor.

TWA remains to be the most common T wave parameter that depends on the repetitive patterns. Current research focused on better time and frequency localisation of alternating sequences [8,10]. In addition to this, Steinbigler et al. considered all periodicities [12]. However, this method depends highly on the signal-to-noise ratio. The spatial variation of the T wave morphology can also be assessed by using simultaneously recorded T waves from different locations instead of consecutive T waves in this method. Couderc et al., on the other hand, used the wavelet transform [13]. The choice of the mother wavelet is critical. They showed that the low order derivatives of Gaussian performed best in separating LQTS patients and normals. Similar research is needed for other patient groups.

Although Padrini et al. did not describe this, the parameters that they used to model T and U waves separately can be used as morphology parameters [14]. Their model is capable of assessing T and U waves separately. Thus it can avoid the uncertainties related to considering these two waves together, which is present in all other methods. Priori et al.'s work, on the other hand, is a clear demonstration of the quantitative use of T wave morphology in understanding ventricular repolarisation abnormalities [15]. Their method is robust and well justified, however CR assesses the repolarization process rather globally. It ignores the source of complexity. The increased 24-hour CR variability, observed in LQTS patients, suggests the use of the 24-hour variability of CR as a separate parameter. Xue et al. showed that CR has a better reproducibility than QT interval measurements [3]. Laguna et al. used a similar method but they used a fixed set of basis functions (principal components) [16]. This set's representativeness of the T wave morphologies determines the performance. The changes in the electrical axis of the heart are likely to degrade its performance due to this dependence.

Badilini et al. performed a PCA analysis to investigate the inter-correlations between the new parameters that they defined [17]. They showed that the T loop has two independent qualities in terms of the in-

formation content: Roundness and planarity. It turned out that QTd and SDQT have almost equal components in both of these, so they are unable to assess them separately. Furthermore, a change in one quality may be compensated by an opposite change in the other and as result neither QTd nor SDQT would show any change. Thus Badilini et al. clearly demonstrated that QTd is a global and indirect measure of ventricular repolarisation heterogeneity. On the other hand, Kors et al.'s choice of T-loop parameters is rather arbitrary [19]. This arbitrariness may explain the small difference in the predictive values of the T-loop and the T-axis. Besides, their definition of the T-axis direction depends on the orientation of the heart [18]. Such a problem can be overcomed by defining vector directions relatively (QRS vector vs. T vector), as Hurst mentioned and was utilised in Acar et al.'s work (TCRT) [20,21]. Acar et al. also introduced the concept of spatial T wave morphology dispersion (TMD). Their temporal variation parameters did not perform as good as the others. These parameters may prove to be useful in some other population.

The vector based parameters are more promising than any of the others. They provide a more profound understanding of the ventricular repolarisation by assessing different qualities of the process at a time, like spatial, temporal variation and morphological complexity. They are more robust than time domain measurements, can be defined independent of subjects (the orientation of the heart) and more immune to noise contamination (by using a sub-space defined by principal components). The beat-to-beat variation of such parameters remains to be explored. On the other hand, time domain parameters (like QTd) are also a measure of heterogeneity and cannot be discarded. The best approach seems to consider as many parameters as available.

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