# Predictive value of ventricular repolarization abnormalities for arrhythmic events

*Aritmik olaylarda ventriküler repolarizasyon anormalliklerinin prediktif değerleri*

*Luigi De Ambroggi*

Department of Cardiology, Policlinico San Donato, University of Milan, Milan, Italy

Many investigations have focused on the key role of ventricular repolarization abnormalities in the genesis of cardiac arrhythmias. Schematically, vulnerability to arrhythmias can arise from two conditions of repolarization process: 1) a state of heterogeneity of repolarization, i.e. a greater than normal dispersion of recovery times, and 2) a dynamic (beat-to-beat) variation of repolarization sequence. This last condition, which frequently occurs in ischemic situations, can be detected by different methods (e.g., analysis of T wave alternans, RR/QT relation variations). The first condition can be detected by analyzing a single beat, using the 12-lead electrocardiogram (ECG) or multiple thoracic leads, i.e. body surface potential maps (BSPM).

## Body surface potential maps

Maps can be recorded with different lead system and various methods of analysis of BSPM have been used to study repolarization potentials.

## Instantaneous potential maps

In normal subjects the potential distribution throughout the ventricular repolarization is usually bipolar, with limited shift of the potential maximum and minimum on the thorax. In some pathological conditions the locations of the potential maximum and minimum can be different than in normal subjects and sometimes, as in myocardial ischemia, a multipolar distribution could be observed during some portion of repolarization (2). This multipolar pattern reflects the complexity of the cardiac generator during that time interval, i.e. the simultaneous presence of multiple regions at quite different potential levels. This situation can favor the reentry phenomenon and thus the initiation of ventricular arrhythmias.

## QRST integral maps

Areas of QRST deflections mainly reflect the intrinsic repolarization properties and are largely independent of ventricular excitation sequence. A complex, multipolar pattern has been related, on the basis of experimental observations, to local heterogeneities of the ventricular recovery process and thus to cardiac states of vulnerability to arrhythmias (3). In our experience, a clear multipolar pattern is visible only in a small percentage of patients affected by ventricular arrhythmias. A multipolar distribution most likely reflects only gross regional inequalities of repolarization, and may not represent a marker sufficiently sensitive for minor disparities.

## Principal Component Analysis

We applied principal component analysis (PCA) to all ST-T waves recorded on the thoracic surface. PCA allows the identification of one set of values, corresponding to the 1st principal component, which better represents most of the original sets of data recorded. Usually the first 3 components provide nearly the total variation of the original data. We proposed to compute the Similarity Index (ratio of first eigenvalue by the sum of all eigenvalues). The value of similarity index is inversely proportional to the variability of T wave morphologies and a low value is considered a marker of repolarization heterogeneity. In our experience, similarity index was found significantly lower than normal in patients affected by congenital LQTS (3), in patients with arrhythmogenic right ventricular dysplasia and ventricular tachycardias (4), and in patients with myocardial infarction and ventricular tachycardias.

## Other repolarization variables (autocorrelation analysis)

In order to analyzing the instantaneous variations of repolarization potentials we proposed two indices: early repolarization deviation index (ERDI) and late repolarization deviation index (LRDI), which express the instantaneous variations of surface potential distributions from the J point to the T peak and from the peak to the end of T wave, respectively (5, 6). We computed these indices in small series of patients with different cardiac diseases (ARVD, LVH due to aortic stenosis, myocardial infarction with and without arrhythmias), and in some groups significant differences from normal subjects were found.

**Address for Correspondence:** Luigi De Ambroggi, MD, Policlinico S: Donato, 20097, San Donato Milanese, Italy, e-mail: luigi.deambroggi@unimi.it

## Conventional 12-lead electrocardiogram

In recent years various methods for quantification of repolarization heterogeneity from the standard 12-lead ECG have been proposed.

## QT dispersion (QTd)

The measurement of 12-lead QT interval dispersion was widely used as an index of repolarization heterogeneity mainly because of its simplicity, but it has several limitations. The major limitation is that this measure can not be related to the "true" spatial heterogeneity of repolarization, since each surface lead is influenced by the electrical activity of the entire heart. Moreover there are other well-known methodological limitations, which can partly explain the controversial results reported in the literature. In summary, whereas initial results coming from small retrospective studies seemed to prove the prognostic value of QTd as risk stratifier, more recent prospective trials did not confirm these data (7, 8). Actually, QTd can be considered only a gross estimate of repolarization abnormalities.

## Principal component analysis

As for BSPM, the method defines several independent components that contain all the information of the T waves of the 12-lead ECG. Okin et al. (9) reported that an increased PCA ratio (2nd /1st component %) was an independent predictor of cardiovascular mortality in a large population of American Indians and in a select diabetic population (10).

## T wave morphology descriptors

In order to identify more precise descriptors of the 12-lead T wave morphology a set of new variables has been proposed (11), that measure the spatial and temporal variations of T wave morphology, the difference of the mean wavefront direction between ventricular depolarization and repolarization, the non-dipolar component. These variables have the advantage to be not critically dependent on time domain measurements (as the identification of T wave end) and showed good reproducibility.

The prognostic value of the total cosine R-to-T (TCRT), an estimate of the angle between repolarization and depolarization wavefront, and the T wave loop dispersion were found significantly associated with clinical events in 261 post-myocardial infarction patients (12).

Another descriptor, the T wave residuum (TWR), that is an index of non-dipolar content of the 12-lead ECG, was found to predict mortality in 772 US veterans with cardiovascular diseases followed-up for 10.4 ± 3.8 years (13). On univariate analysis, patients with T wave residua above the median value had significant worse survival compared to patients with values below the median.

In conclusion, several variables can describe, with different degree of accuracy, the "complexity" of the surface T waves that most likely reflects heterogeneities of the repolarization process in the heart, which in turn play a role in the arrhythmogenesis.

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