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Beat-to-beat ventricular repolarization variability evaluated during acute myocardial ischemia☆

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ABSTRACT

Experimental and clinical studies have shown that beat-to-beat variability of ventricular repolarization morphology, which can be measured by T-wave spectral variance (TSV) index based on the two-dimensional Fourier transform, is associated with an increased risk of developing malignant ventricular arrhythmias.

In the present study we tested TSV index during percutaneous coronary intervention (PCI) procedure in the 12 standard ECG leads and in the orthogonal *X*, *Y* and *Z* leads. In addition, we analyzed the intrasubject and intersubject variability of TSV index, in order to determine reliable limits of significant repolarization variability due to an ischemic cardiac process. A total population of 62 patients, in which two ECG controls and one ECG recording during PCI procedure, were obtained. Results indicate that TSV index showed significant differences during PCI procedure with respect to control situation in all ECG leads ($p < 0.0001$).

The relative change between PCI procedure and control situation showed that there is a preferential ECG lead to analyze the TSV index depending on the occlusion site. Moreover, TSV index presented a high stability in each patient and a significant larger variability among patients. Finally, we conclude that TSV index offers a robust tool for evaluating beat-to-beat repolarization variability during acute myocardial ischemia.

1. Introduction

Ventricular repolarization dispersion (VRD) is a measure of inhomogeneous recovery of excitability during repolarization process. This ventricular heterogeneity is mainly attributable to differences in activation times and action potential duration (APD) in different heart areas. The APDs differs not only between myocytes of different ventricular layers [1] but also between posterior and anterior endocardial layers, apex and base [2], and left and right ventricles [3]. Thereby, increments in VRD values that are higher than normal are associated with an increased risk of developing reentrant arrhythmias [4,5].

Experimental and clinical studies have demonstrated a relationship between VRD and severe ventricular arrhythmia and/or sudden cardiac death [6,7]. Also, it was shown that modifications in the morphology of the T-wave are associated with an increased VRD [8,9]. Several techniques have been presented to analyze and quantify the temporal variability of ventricular repolarization [10,11]. Moreover, beat-to-beat measurement of the QT interval is based on the exact delineation of the T-wave end point, which frequently fails in automatic ECG analysis [12,13]. Low level beat-to-beat variations in ventricular repolarization (both amplitude and/or time duration) can be detected by using high resolution techniques in ECG recordings [14]. Also, the beat-to-beat changes were evaluated by using the T-wave spectral variance (TSV) index method, based on the two-dimensional Fourier transform (2D-FFT), which allows to detect dynamic changes in the repolarization pattern independently of the exact definition of the end point of the T-wave [15–17].

Steinbigler et al. showed that TSV index reveals an increased VRD in patients prone to ventricular tachycardia and ventricular fibrillation after myocardial infarction, while the corrected QT interval showed no signficant differences [15]. On the other hand, Valverde et al. observed that TSV index detects the presence of temporal repolarization variability in a model of chronic infarcted animals [16]. Later, in another work, Steinbigler et al. showed that TSV index was significantly higher in patients with idiopathic dilated cardiomyopathy prone to ventricular fibrillation respect to no ventricular fibrillation group [17]. However, all these authors did not study the TSV index in different ECG projections. As far as

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we know, there are no results indicating the role of the TSV index from different ECG leads by other authors. Moreover, we analize the TSV index in different ECG projections during acute myocardial ischemia induced by percutaneous coronary intervention (PCI) procedure. The TSV index can be calculated without the necessity of exact delineation of the T-wave endpoint and it might allow the detection of spatial ventricular repolarization dispersion if enough numbers of leads were used in the ECG acquisition [15].

The aims of this work were to: (1) Evaluate the presence of beat-to-beat repolarization variability during PCI procedure in the 12 standard ECG leads and in the orthogonal *X*, *Y* and *Z* leads. (2) Analyze the intrasubject and intersubject variation of TSV index at control ECG recordings before PCI procedure. (3) Conclude the advantages and disadvantages of TSV index during acute myocardial ischemia to optimize cardiac risk stratification of patients which might enable a better treatment and a good improved short and long-term prognosis.

2. Materials and methods

2.1. Database

In the present work we used the STAFF III database, which comprised 108 patients obtained from the Charleston Area Medical Center in West Virginia, receiving elective PCI (nonperfusion balloons) in one of the major coronary arteries (STAFF III study). Twenty-five patients were excluded from further analysis because they suffered from ventricular tachycardia, had undergone an emergency procedure or presented signal loss during ECG acquisition. A population of 83 patients was included, 55 males and 28 females, ages 32–78 years (mean 60 ± 12 years). The population consist of: *leftmain* (LM) occlusion artery in 2 patients, *leftanteriordescending* (LAD) coronary occlusion artery in 28 patients, *rightcoronaryartery* (RCA) occlusion in 37 patients and *leftcircumflex* (LCx) coronary occlusion artery in 16 patients. The study was approved by the local investigational review board, and informed consent was obtained from each subject before enrolment. A data form indicating the anatomic site and the exact times of inflation and deflation of the balloon was completed. If a patient received more than one balloon inflation during the same procedure, only the first inflation was considered. The mean inflation duration was 4 min 28 s with a standard deviation of 74 s. Eight leads (v1-v6, I, II) were recorded using equipment by Siemens-Elena AB (Solna, Sweden) and digitized at sampling rate of 1000 Hz and amplitude resolution of 0.6 μV. Leads III, aVR, aVL and aVF were derived from leads I and II. Synthesized orthogonal *X*, *Y* and *Z* leads were obtained by the Kors transform [18] obtaining a total of 15 ECG leads.

Three ECG records were acquired for each patient. First, two control recordings were acquired continuously for five min in supine position prior to the PCI procedure in clinical stable conditions, within a time interval of maximum 1 hour in the room and/or catheterization laboratory. The electrodes were maintained on the patients between both recordings with their positions marked, to enable accurate comparisons of the ECG variables. Second, one continuous ECG was recorded during PCI procedure, starting before and ending after balloon inflation and deflation respectively. Therefore, the patients behaved as their own controls. One example of ECG recordings for a particular patient of the STAFF III database before (control situation) and during PCI procedure is shown in leads I (Fig. 1a), v2 (Fig. 1b) and *X* (Fig. 1c).

2.2. ECG preprocessing

We applied a signal pre-processing to the 15 leads ECG records during control and PCI procedure respectively. Both controls and PCI ECG records were filtered with a notch filter (Butterworth, 2nd order, 60 Hz) to minimize the power-line interference. A cubic spline interpolation filter was used to attenuate ECG baseline drifts and respiratory artifacts [19]. Thereafter, QRS complexes and their endpoints were detected in each ECG-lead using a modified version algorithm proposed by Pan and Tompkins [20].

In each ECG lead (both controls and PCI procedure), one QRS template was constructed by calculating the median of the total QRS complexes. After that, if the cross-correlation coefficient between QRS complexes and each QRS template was greater than 98%, a new jitter-corrected QRS complex is obtained, otherwise the complex was rejected. Taken 80 ms from fiducially jitter-corrected QRS endpoint, a T-wave window of 250 ms duration was defined in order to construct an aligned T-waves matrix (Fig. 2a). This determined the input matrix containing arranged T-waves for the 2D-FFT process, as can be observed in Fig. 2b.

2.3. T-wave spectral variance index

We computed the TSV index with an algorithm described by Steinbigler et al. [15]. The basement of the algorithm is the 2D-FFT. First, a one-dimensional FFT (1D-FFT) is applied to each T-wave of the T-waves matrix, and the frequency contents were determined. The result is a matrix containing the power spectrum of each T-wave, in which the *x*-axis correspond to the frequency content in Hertz and the amplitude (*z*-axis) correspond to the magnitude of the power spectrum expressed in μV^2. A second 1D-FFT is applied to the assembly of the power spectrum of each T-wave in order to evaluate the periodic appearance of each frequency content (y-axis), expressed in cycles-per-beat (cpb), as shown in Fig. 2c.

Steinbigler et al. considered the frequency content of the T-wave less than 50 Hz, and they calculated the TSV index as a non-units (n.u.) ratio of the spectral energy with beat-to-beat variability greater than 0 cpb and the total spectral energy, from 0 Hz to 50 Hz [15]. This assumption is supported by Thakor et al., who separated the power spectrum of the QRS complexes and, P- and T-waves in healthy and abnormal patients, and observed that the power spectrums of these complexes and waves were less than 40 Hz [21]. In consequence, we computed the beat-to-beat variability of the T-wave less than 50 Hz as following:

$$TSV = \left.\frac{\text{Spectral Energy} > 0\text{cpb}}{\text{Total Spectral Energy}}\right|_{<50\,\text{Hz}} \quad (1)$$

A TSV index near 0 is indicative of a constant T-wave morphology in all the beats included for the analysis. In contrast, if different degrees of variability in the shape of the T-wave are present, the TSV index tends to 1. Beat-to-beat variability appearing at frequencies from 50 Hz to 100 Hz can be considered as noise because no spectral components of the T-waves appear at these frequencies. We evaluated the noise/T-wave amplitude ratio (NTR) in this technique as the ratio between the total spectral energy from noise bandwidth respect to the total spectral energy of the T-wave [16].

$$NTR = \frac{\text{Total Spectral Energy}\,(50\text{–}100)\,Hz}{\text{Total Spectral Energy} < (50)\,Hz}. \quad (2)$$

2.4. Exclusion criteria of ECG recordings

Those patients who have shown at least one T-waves matrix with less than 64 consecutive T-waves were rejected. The noise ratio was obtained for each matrix and those patients with a NTR greater than 0.30 times were considered noisy and rejected. Using these exclusion criteria, a total population (TP) group of 62 patients in this work were analyzed. Finally, the location of 62 balloon inflations were: LM in 2 patients, LAD in 21 patients, LCx in 12 patients and RCA in 27 patients.