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Beat-to-beat electrocardiographic analysis of ventricular repolarization variability in patients after myocardial infarction ☆

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Abstract Several studies have shown that the beat-to-beat variability of ventricular repolarization, which can be computed by T-wave spectral variance (TSV) index, constitutes a marker of cardiac risk. Moreover, the fact that properties of action potential duration are altered during the healing (days, weeks) and healed (months) infarct stages, have been reported. However, no data exist regarding the influence of the time elapsed after myocardial infarction (MI) on modulation of the beat-to-beat ventricular repolarization variability.

In the present work we have evaluated TSV index during healing and healed stages of MI using 12 standard ECG leads. The ECG of control or healthy subjects (n = 49) and the ECGs in patients after MI (n = 38), one within the first seven days (MI_7) and the other after 60 days (MI_{60}) of cardiac infarction, have been analyzed.

We have considered the *preferential ECG leads* as those leads in which TSV index have presented a relative change greater than 10 in MI_7 respect to control. Results indicate that TSV index have shown a significant increase ($p < 0.0005$) in I, II, aVR, aVF, V3, V4, V5 and V6 leads in healing phase of MI (MI_7) with respect to control. Further, in the healed phase of MI (MI_{60}), the TSV index tends to decrease their values towards the control. Also, we have computed a multilead TSV index based on the *preferential ECG leads*. In that sense, the multilead criteria have shown better perfomance quantifying beat-to-beat repolarization variability than any single ECG lead considered. The sensitivity, specificity and AUC of TSV index were: 92%, 90% and 0.96 for MI_7; and 76%, 84% and 0.81 for MI_{60}, respectively. Moreover, the beat-to-beat ventricular repolarization variability has been quantified by the QT variability index (QTVI). Even though the results that we have obtained with TSV index have been comparable to those obtained with the QTVI, this latter has not reflected the modulation effect associated to time elapsed after MI. Also, the *preferential ECG leads depending on MI site* using TSV index have been computed, being lead V4 for anterior and lead aVF for inferior MI, respectively. Finally, this study might help understand the role of healing and healed stages following MI on beat-to-beat variability modulation of ventricular repolarization.

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Introduction

It has been recognized that after myocardial infarction (MI), patients have a high incidence of ventricular arrhythmias and sudden cardiac death [1]. Also, persistent modifications of heterogeneity of ventricular repolarization constitutes a further important cardiac risk indicator in patients with ischemic heart disease [2]. Further, it has demonstrated that various arrhythmic phases occur after the onset of induced MI [3]. The strongest hypothesis, supported by experimental results, suggests that cardiac arrhythmia can be explained as a consequence of alterations in electrical activity in specific zones of the heart after MI [3]. During the healing (days, weeks) or healed (months) stages of MI, sustained ventricular tachycardias are inducible [4]. This phenomenon suggests the existence of reentry pathways and conduction block in different phases of MI.

Ventricular repolarization is a complex process that varies in duration from beat-to-beat. In this sense, several clinical investigations have studied beat-to-beat variability in QT interval as a means of quantifying temporal repolarization lability [5–7]. On the other hand, it has shown that modifications in the morphology of the T-wave are associated with an increase of repolarization heterogeneity [8,9]. There is evidence that low level beat-to-beat variations in ventricular repolarization can be measured 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 [10–13]. Steinbigler et al. showed that TSV index

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revealed an increased heterogeneity of the ventricular repolarization in patients prone to ventricular tachycardia (VT) and ventricular fibrillation (VF) after MI in two standarized Holter orthogonal leads, while the corrected QT interval showed no significant differences [10]. Also, Valverde et al. studied the temporal evolution of TSV index in a single ECG lead using a model of chronic infarcted animals [11]. Later, in another work, Valverde et al. found that there was a preferential ECG lead to analyze the TSV index depending on the occlusion site during a percutaneous coronary intervention procedure [13].

Based on the studies cited above we propose to understand the relationship between healing and healed infarct phases and the beat-to-beat ventricular repolarization variability. Therefore, the aims of this work were to: (1) analyze the MI phases using TSV index and evaluate the *preferential ECG leads* to apply a multilead criteria; (2) study the *preferential ECG leads depending on MI site*; (3) show a comparison between the TSV index and QT variability index and evaluate advantages and disadvantages of both.

Materials and methods

Dataset

The Physikalisch-Technische Bundesanstalt (PTB) ECG database which is available free on the Physio-Bank [14] was used. This data set comprises 52 healthy subjects and 148 MI patients. The ECGs were digitized at 1000 samples per second, with 16 bit resolution over a range of ±16.384 mV with 2000 A/D units per mV. Each record includes 12 simultaneously conventional ECG leads.

We have selected the following data subsets, according to the detailed clinical summary included in the PTB database [15]: the ECG of healthy subjects (control), $n = 49$ (37 males and 12 females, 43±14 years old), and those infarcted patients without documented ventricular tachycardia (VT) and/or ventricular fibrillation (VF), which simultaneously comprise two ECGs recordings, $n = 38$ (31 males and 7 females, 55±10 years old): one record within the first seven days (MI_7, healing phase) of MI, and the other 60 days (MI_{60}, healed phase) after MI. Concerning the location of myocardial infarction they were in: anterior ($n = 2$), antero-lateral ($n = 7$), antero-septal ($n = 11$), inferior ($n = 10$), infero-lateral ($n = 6$), infero-postero-lateral ($n = 1$) and posterior ($n = 1$).

Moreover, with the aim to analyze the TSV index in the *preferential ECG leads depending on MI site*, we have grouped MI patients without VT/VF into two sets: those patients who have presented the anterior area affected, $n = 20$: anterior ($n = 2$), antero-lateral ($n = 7$) and antero-septal ($n = 11$); and those patients who have infarcted the inferior area, $n = 17$: inferior ($n = 10$), infero-lateral ($n = 6$), infero-postero-lateral ($n = 1$).

None of the subjects analyzed had presented bundle branch block or intra-ventricular conduction defects. The QRS durations for healthy subjects were comparable with patients with MI. The data have been studied anonymously, using publicly available secondary data, therefore no ethics statement is required for this investigation [14].

ECG preprocessing

We applied a signal pre-processing to the 12 leads ECG records of all subsets. The ECG records were filtered with a notch filter (Butterworth, 2nd order, 50 Hz) to minimize the power-line interference. A cubic spline interpolation filter was used to attenuate ECG baseline drifts and respiratory artifacts [16]. After that, QRS complexes and their endpoints were detected in each ECG-lead using a modified version algorithm proposed by Pan and Tompkins [17].

A QRS template was constructed by calculating the median of the total QRS complexes for each ECG lead. 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 [13]. This determined the input matrix containing arranged T-waves for the 2D-FFT process. Besides, we have considered choosing the T-wave window size. For that matter, we have computed for each subject and for each ECG lead the T-wave width using a wavelet-based ECG delineator [18]. Then, we can observe that a window of 250 ms has been enough to cover the total of ventricular repolarization process in control, MI_7 and MI_{60}, respectively.

T-wave spectral variance index

We computed the TSV index using the algorithm described in [12], which was modified by Valverde et al. in [13]. Briefly, a one-dimensional FFT (1D-FFT) is applied to each T-wave of the T-waves matrix, and the frequency contents were determined. With the aim to avoid edge discontinuities, the input data was previously multiplied by a Blackman window. 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).

We have 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. In consequence, we computed the beat-to-beat variability of the T-wave less than 50 Hz as following:

$$\mathrm{TSV} = \left.\frac{\mathrm{spectralenergy}_{>0\ cpb}}{\mathrm{totalspectralenergy}}\right|_{<50\ Hz} \quad (1)$$

Also, we have evaluated the noise/T-wave amplitude ratio (NTR) between the spectral energy from noise bandwidth (50–100 Hz) respect to the spectral energy of the T-wave (0–50 Hz), both greater than 0 cpb [13].

$$\mathrm{NTR} = \left.\frac{\mathrm{spectralenergy}(50-100\ \mathrm{Hz})}{\mathrm{spectralenergy}(<50\ Hz)}\right|_{>0\ cpb} \quad (2)$$

Those patients who had 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.

Relative changes of TSV index and multilead criteria

The mean value $\overline{TSV}^{C}$ for each lead was obtained for control subjects, and in the same way, $\overline{TSV}^{MI_7}$ and $\overline{TSV}^{MI_{60}}$ were calculated. The results were presented as mean ± standard error of the mean (SEM).

Also, for each ECG lead, the relative change bewteen MI_7 and control group was defined as

$$\mathscr{R}^{\mathrm{MI}_7} = \frac{\overline{TSV}^{\mathrm{MI}_7}}{\overline{TSV}^{C}} \tag{3}$$

and likewise,

$$\mathscr{R}^{\mathrm{MI}_{60}} = \frac{\overline{TSV}^{\mathrm{MI}_{60}}}{\overline{TSV}^{C}} \tag{4}$$

was computed.

Based on the relative change analysis, we selected the *preferential ECG leads* as those leads which have a $\mathscr{R}^{MI_7}$ >10. Moreover, we prosposed for each subject a multilead criteria (ML) which was computed as:

$$TSV_{ML}^{C} = \frac{1}{M}\sum_{i=1}^{M} TSV_{i}^{C} \tag{5}$$

for control situation, where $i = 1...M$ are the so called *preferential ECG leads*. In the same way, $TSV_{ML}^{MI_7}$ and $TSV_{ML}^{MI_{60}}$ were obtained. Also, mean values $\overline{TSV}_{ML}^{C}$, $\overline{TSV}_{ML}^{MI_7}$ and $\overline{TSV}_{ML}^{MI_{60}}$ were calculated.

Preferential ECG lead depending on myocardial infarction site

We evaluated two sets of patients: anterior and inferior MI as we have shown in Subsection 2.1. We studied the dependence of the ECG leads according the site of myocardial damage. In this sense we have computed the TSV index applying the following criteria: firstly, the Relative Change in MI_7 must be the maximum and in MI_{60} must be less than 10 simultaneously; secondly, the TSV index difference between control and MI_7 and between control and MI_{60} must be statistically significant.

QT variability index

In order to compare the TSV index with another standardized method which quantify beat-to-beat repolarization variability, the QT variability index (QTVI), was calculated [5]. QTVI quantifies the magnitude of QT interval fluctuations, normalized by both the mean QT duration and the magnitude of heart rate fluctuations. In order to calculate the QTVI, the beginning of the QRS complex and the end of the T-wave were measured by using a modified version of the wavelet-based ECG delineator proposed by Martinez et al. [18]. For each subject, an unique QTVI was obtained as the mean value of the QTVI obtained from all the ECG leads. We introduced this unique value in order to avoid the inconvenience of selecting different ECG leads for each patient as was implemented in [5–7]. Analysis of QTVI were made with control, MI_7 and MI_{60} groups (see Section 3).

Statistical analysis

In order to determine the statistical significance of TSV index between control, MI_7 and MI_{60}, the TSV was calculated for each patient and for each lead. D'Agostino-Pearson normality test was applied with the aim of quantify the discrepancy between the distribution of TSV index an ideal Gaussian distributions. Moreover, in order to evaluate the influence of the heart rate in the estimation of T-wave variability, we analyzed the RR interval along the total beats considered for control situation, MI_7 and MI_{60}. Mean values of RR intervals for all subsets were obtained by averaging the mean RR interval of each subject. Non-parametric two-sided Mann–Whitney U test was used in a unpaired samples, and the Wilcoxon sign rank test was used in paired samples. When p value was < 0.05, differences were considered statistically significant.

To evaluate the performance of the TSV index, we computed Sensitivity, Specificity and Area under curve (AUC) for MI_7 and for MI_{60} groups, both respect to the healthy subjects.

Results

The TSV was calculated during control, MI_7 and MI_{60} subsets. A non-parametric two-sided Mann–Whitney U test was used between control and MI_7 and also between control and MI_{60}. A Wilcoxon sign rank test was used between MI_7 and MI_{60}. The mean ± SEM of the TSV values, for each lead, with their statistical significant differences are presented in Fig. 1.

Relative changes of TSV index for both MI_7 and MI_{60} respect to healthy subjects, for each lead, are shown in Fig. 2. We have observed that the *preferential ECG leads* were: frontal leads I, II, aVR, and precordial leads V4, V5.

Multilead criteria showed $\overline{TSV}_{ML}^{C} = 0.011 \pm 0.002$, $TSV_{ML}^{MI_7} = 0.212 \pm 0.035^{\ddagger *}$ and $\overline{TSV}_{ML}^{MI_{60}} = 0.117 \pm 0.020^{\dagger}$, all expresed as mean ± SEM, being ‡ $p < 0.0005$ and † $p < 0.05$ for MI_7 and MI_{60} respect to control situation. * $p < 0.05$ between MI_7 and MI_{60}. *Sensitivity vs. 1-Specificity* curves for the *preferential ECG leads* and ML are shown in Fig. 3 for both MI_7 and MI_{60} groups respect to control situation.

Table 1 shows the Sensitivity, Specificity and AUC of TSV indexes for each lead and ML for MI_7 and MI_{60} groups respect to healthy subjects.

Table 2 shows the TSV index (mean ± SEM), the relative change, the Sensitivity, Specificity, AUC and the *preferential ECG leads depending on MI site* obtained to separate both anterior and inferior groups respect to healthy subjects considering the MI_7 and MI_{60} stages.

The QTVI (mean ± SEM), expressed in non-units, showed significant differences between control (−1.31± 0.07) and MI_7 (0.14±0.12), $p < 0.0005$. In the same manner,

the QTVI showed significant differences between control and MI_{60} (−0.19±0.14), $p < 0.0005$. Sensitivity, Specificity and AUC are shown in Table. 1. There was no significant statistical difference between MI_7 and MI_{60}.

In Fig. 4 it can be observed a particular patient in which the power spectrum shows a decrement of the energy at all the periodicites except to 0 cpb for MI_{60} (Fig. 4f) respect to MI_7 (Fig. 4e), resulting in a lesser TSV index in MI_{60} stage respect to MI_7 stage. Also, in the same figure, it can be observed the power spectrum of a healthy subject (Fig. 4d).

The RR interval (mean ± SEM) showed significant differences between MI_7 (730±19 ms) and both control (896±21 ms) and MI_{60} (843±19 ms), $p < 0.0005$ respectively. There was no significant statistical difference between control and MI_{60}.

The QRS duration (mean ± SEM) showed non-significant differences between control (84±1 ms) and both MI_7 (87±2 ms) and MI_{60} (89±2 ms), $p = NS$ respectively. There was no significant statistical difference between MI_7 and MI_{60}.

Discussion

It is known that healed MI phase is the most frequent clinical setting for the development of sustained VT. However, the first episode of VT may occur years after MI healing, often without apparent clinical evidence [19]. Consequently, the range is broad, ranging from tolerated sustained VT to sudden cardiac death. Also, it is probable that several events need to coincide for a cardiac arrest, an underlying susceptibility to VT/VF due to myocardial scar, abnormalities in cardiac conduction and repolarization along with alterations in autonomic modulation [20]. Moreover, it has been recently evaluated the association of electrocardiographic repolarization and depolarization patterns to vulnerability to ventricular tachyarrhythmias [21]. Results showed that abnormalities in ventricular depolarization are more common among post- MI patients with prior VT/VF than in those without documented ventricular tachyarrhythmias. Simultaneously, it has been shown that abnormal T-wave morphology and T wave alternans seem to reflect the heart disease rather than specifically vulnerability to VT/VF [21].

In the present work, when we analyzed the *preferential ECG leads*, it was observed an increment of TSV index in MI_7 and a tendency to decrease in MI_{60} with respect to normal subjects. In the same manner, in [11], the animal model has shown a similar TSV index behavior between 15 and 45 days after surgery in comparison with control situation. Both evidences could be associated to the idea that the TSV index suffer some kind of modulation for two stages of MI: first, in the healing stage of MI (MI_7) with an abrupt increase of TSV index and later, in the healed phase of MI (MI_{60}) with a tendency to decrease the TSV index toward control values.

Analysis of TSV index in MI_7

We observed that $\overline{TSV}^{MI_7}$ compared against $\overline{TSV}^{C}$ was statistically significant for all the ECG leads but were not to lead III and V2, as can be observed in Fig. 1. These results suggested that beat-to-beat variability index could not be strongly dependent to the ECG lead analyzed within the first seven days of MI. However, in a more exhaustive analysis of TSV index, we found that *preferential ECG leads* reached maximum values of relative change ranging from 13 up to 29 (see Fig. 2). In concordance with the aforementioned results, we observed that Sensitivity ranging from 76% up to 84%, Specificity ranging from 71% up to 88% and AUC ranging from 0.84 up to 0.93, as can be observed in Table 1.

The reason why the beat-to-beat repolarization is modified is not easy to explain, but an hypothetical explanation may be offered. The epicardial border zone (EBZ) [4,22], is a specific region prone to cause VT/VF during healing phase. In this stage, *electrical remodeling* increases the connective tissue and edema leading to nonuniform anisotropy [3], which can produce reentry

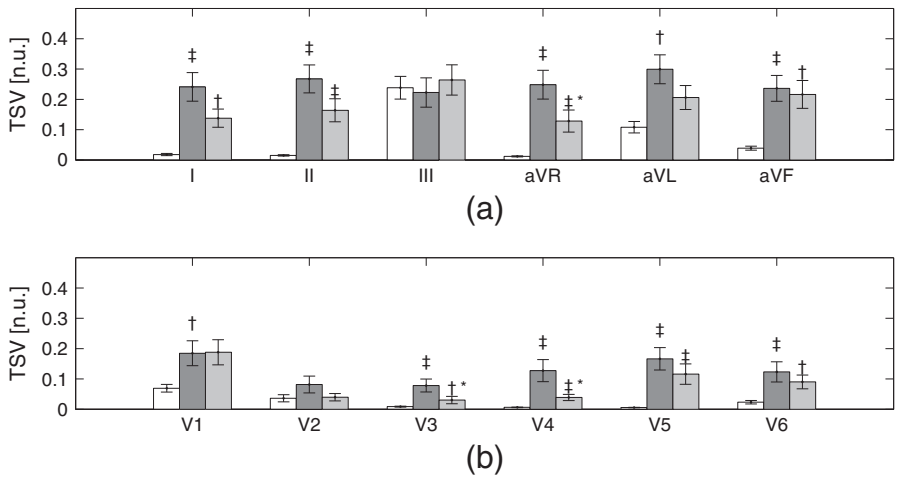

Fig. 1. Bar graph showing healthy subjects (white bars), first seven days of MI (dark gray bars) and after 60 days of MI (light gray bars) TSV indexes, expressed in non-units, as mean ± SEM for each lead. (a) frontal ECG leads and (b) precordial ECG leads. †$p < 0.05$, ‡$p < 0.0005$ respect to control group. *$p < 0.05$ indicates statistical significant differences of TSV index between MI_7 and MI_{60}.

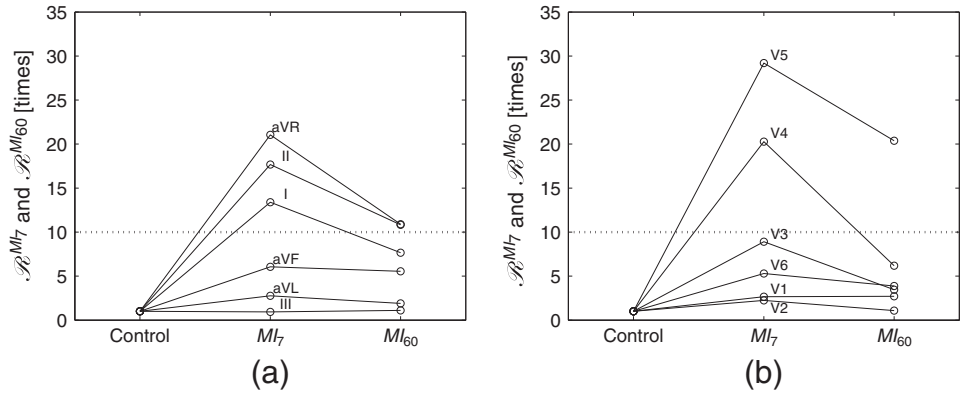

Fig. 2. Relative change, expressed in times for the whole population, for the MI_7 subset ($\mathscr{R}^{MI_7}$) and for the MI_{60} subset ($\mathscr{R}^{MI_{60}}$) respect to the control group, for each lead. (a) shows the frontal ECG leads and (b) shows the precordial ECG leads.

pathways and conduction block thus increasing cardiac risk. Moreover, it has shown that *electrical remodeling* after MI is not only confined to EBZ, but also can be extended to noninfarcted regions of myocardium, producing a marked heterogeneity of repolarization over the course of time [23]. Also, in vivo experiments during healing stage have presented fractionated electrograms that have produced slow and discontinuous activation which has often changed from beat-to-beat [24].

Therefore, we could hypothesize that these inhomogeneities in the course of time could be translated to the TSV index changes. The aforementioned hypothesis can be reinforced when the beat-to-beat repolarization variability was quantified and evaluated utilizing the QT interval. In this sense it has been denoted that the QT variability is influenced by several factors that play different roles depending on structural and cardiac electrical remodeling as it showed in [25].

Analysis of TSV index in MI_{60}

We observed that $\overline{TSV}^{MI_{60}}$ compared against $\overline{TSV}^{C}$ was statistically significant for all the ECG leads but was not to lead III, aVL, V1 and V2 as can be observed in Fig. 1. In addition, in the analysis of *preferential ECG leads*, all were significantly different when TSV index was contrasted between control and MI_{60}. Furthermore, the relative change, $\mathscr{R}^{MI_{60}}$, was greater than 10 for II, aVR and V5 leads, but not for leads I and V4. Simultaneously to the results presented above, it can be noted that $\mathscr{R}^{MI_{60}}$ have decreased respect to $\mathscr{R}^{MI_7}$, as we can see in Fig. 2. Also, it can be highlighted that leads aVR, V3 and V4 are statistically different when compared $\overline{TSV}^{MI_7}$ respect to $\overline{TSV}^{MI_{60}}$. All these results denoting that after 60 days of MI, the TSV indexes for the *preferential ECG leads* tend to decrease their values toward the control situation. Also, the Sensitivity ranged from 66% up to 76%, Specificity ranged from 69% up to 82% and AUC ranged from 0.72 up to 0.84, as can be observed in Table 1. Due to the TSV index in MI_{60} remains greater respect to healthly subjects but lesser than MI_7 we could suppose that beat-to-beat variability index could be a marker of silent infarct or lesser ischemia area in the ventricles, phenomena which is expressed in the form of subtle microvolt level changes in the T-wave morphology.

On the other hand, one experimental study has compared healing (1–2 weeks) and healed (2–16 months) phases of MI

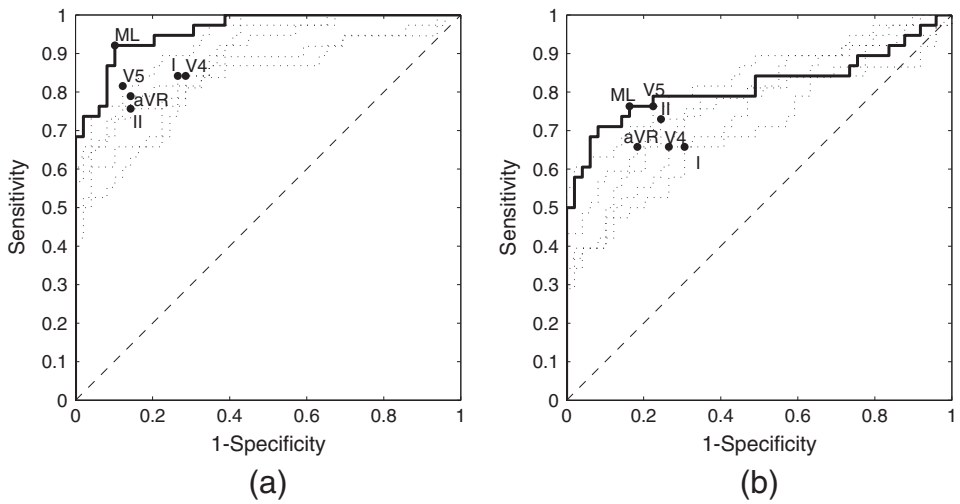

Fig. 3. *Sensitivity vs. 1-Specificity* curves for the *preferential ECG leads* (dotted line) and ML (solid line). The optimal TSV threshold for each considered lead and ML are located at the filled circles. a) MI_7 respect to control group and (b) MI_{60} respect to control group.

Table 1
Sensitivity and specificity, expressed in percent and AUC, expressed in non-units, of TSV indexes for each lead, ML and QTVI for both MI_7 and MI_{60} groups respect to healthy subjects.

		I	II	III	aVR	aVL	aVF	V1	V2	V3	V4	V5	V6	ML	QTVI
MI_7	Sens	84	76	31	79	53	76	55	63	74	84	82	63	92	88
	Spec	73	86	72	86	84	71	61	51	67	71	88	78	90	92
	AUC	0.84	0.86	0.44	0.90	0.65	0.77	0.65	0.61	0.76	0.86	0.93	0.78	0.96	0.95
MI_{60}	Sens	66	73	37	66	47	54	50	58	61	66	76	82	76	82
	Spec	69	76	72	82	71	78	65	53	67	73	78	51	84	82
	AUC	0.72	0.77	0.49	0.76	0.59	0.67	0.58	0.53	0.67	0.75	0.84	0.71	0.81	0.88

[22]. They have observed that in this latter phase the APD profiles returned to almost normal values, suggesting the presence of a process that has been denominated *reverse remodeling* in concordance with another studies [26,27]. Also, it has been shown the existence of characteristics of beat-to-beat variability at the onset and offset of the QRS complex [28], results that may correlate with myocardial electrical instability and clinically important predictive value for ventricular arrhythmias. Considering the following studies [26–28], our results support the hypothesis that, in healed phase of MI there is certain decrement of APD differences in the course of time (i.e. profiles returned to nearly normal), phenomenon that could be translated to a decrease of TSV index.

Evaluation of multilead criteria

With the aim to obtain an unique estimation of beat-to-beat variability in infarcted patients, we have computed a mean value of TSV using *preferential ECG leads*. In this sense, the multilead criteria have shown better results than any single ECG lead evaluation of Sensitivity, Specificity and AUC, as we can be observed in Fig. 3 and in the Table 1 (92%, 90% and 0.96 for MI_7 and 76%, 84% and 0.82 for MI_{60}).

Selection of the preferential ECG leads based on site of MI

When patients were studied according to the infarcted area we have observed that the *preferential ECG leads depending on MI site* were lead V4 for anterior and lead aVR for inferior groups respectively (see Table 2).We denote that even though there are leads of the ECG according to the site of MI, the multilead criteria reached better values of Sensitivity, Specificty and AUC than those obtained from the *preferential ECG leads depending on MI site*, as we can observe comparing Tables 1 and 2.

Table 2
Mean TSV value ± SEM, expressed in non-units, Relative change, expressed in non-units, Sensitivity and Specificity, expressed in percent, AUC, expressed in non-units and the *preferential ECG leads depending on MI site*, considering the anterior and inferior groups respect to healthy subjects, being ‡ $p < 0.0005$ and † $p < 0.05$ for MI_7 and MI_{60} respect to control situation.

		$\overline{TSV} \pm SEM$	$\mathscr{R}$	Sens	Spec	AUC	Lead
Anterior	MI_7	0.141±0.056‡	22	90	73	0.90	V4
	MI_{60}	0.054±0.017‡	9	70	90	0.81	
Inferior	MI_7	0.250±0.078‡	21	76	80	0.86	aVR
	MI_{60}	0.081±0.036†	7	76	69	0.76	

Comparison between TSV index and QTVI

It can be seen in Table 1, that TSV index for ML criteria has shown greater sensitivity for MI_7 and greater specificity for MI_{60} than QTVI. Moreover, QTVI has shown greater specificity for MI_7 and greater sensitivity for MI_{60} than TSV index for ML criteria. Also, both indices have shown statistically significant differences between control and MI_7 and MI_{60} respectively. Moreover, TSV index for ML criteria has shown statistically significant differences between MI_7 and MI_{60} while the QTVI has not detected differences between MI_7 and MI_{60} (p = NS). Therefore, the TSV has shown the effect of modulation over beat-to-beat variability caused by the time elapsed after MI, as we have previously observed in an animal model in [11].

Previously described techniques for automated beat-to-beat QT interval assessment are largely based on criteria to detect T-wave end position, in consequence the QT measurement is highly dependent on waveform morphology, when the signal is low in amplitude and slope. Therefore it can be possible to introduce erroneous measurements [10–29,31]. In contrast, Berger et al. [5] proposed the QT variability as a robust technique insensitive to inaccuracies in QT interval measurements using the compressing or stretching of the JT segment of every beat in analyzed epoch to match template. Also, with TSV technique the repolarization variabilities not only do we obtain the changes of intervals defined by T-wave peak or T-wave end position, but also the morphological changes of the entire repolarization process during MI. Then, the use of the ML criteria can offer a robust tool to compute the beat-to-beat repolarization variability.

Study limitations

We have proposed this preliminary study in order to pave the way for further clinical research. Therefore, further clinical trials will be helpful to better assess the accuracy of the TSV index in identifying patients at risk for arrhythmic events during healing and healed stages of MI.

Unfortunately, the PTB database does not contain additional imaging or electrophysiological studies, then we have used the time elapsed after MI as indicator of two different stages (healing and healed), mainly we have based

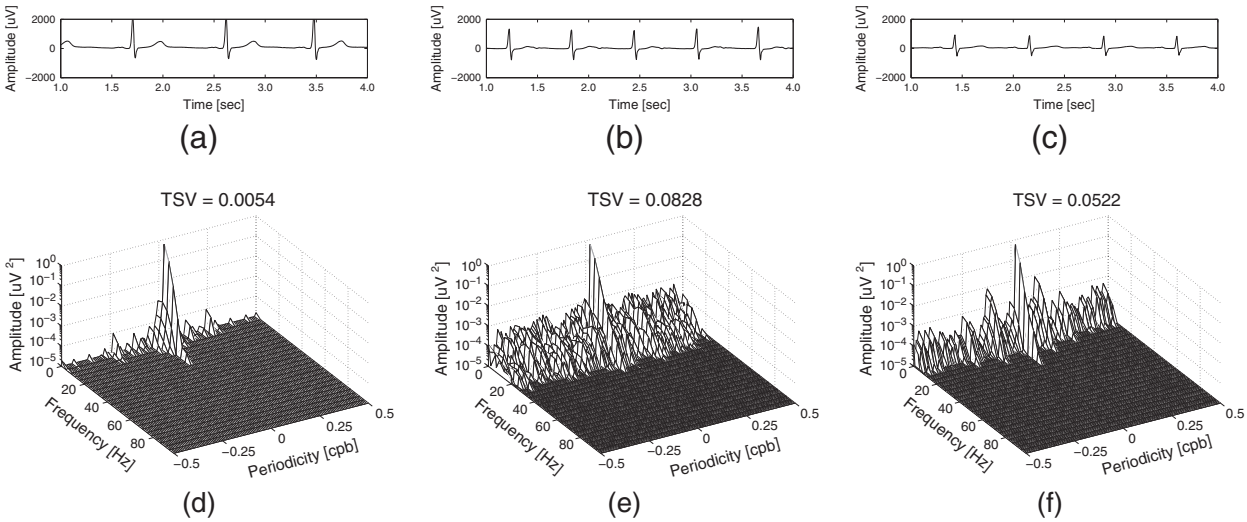

Fig. 4. Power spectrum amplitude of the 2D-FFT represented in a logarithmic scale for a healthy subject and a particular patient (bottom panels), including a portion of their associated ECG records for V4 lead (upper panels). (a) and (d) shows control subject. In (b) and (e) it can be observed the MI_7 stage. (c) and (f) shows MI_{60} stage.

this issue on several works of cardiac electrophysiology [3,4] and clinical evidences [19–21].

The 2D-FFT technique does not suppress noise, in consequence, reliable results depend on a low noise/T-wave amplitude ratio.

Although we have applied a T-wave duration window that has been large enough to cover the total ventricular repolarization phase (see Section 2.1), we should reconsider the length of this window in a future works, for example in patients with LQTS [32,33].

Conclusions

The most important finding of the present work is the influence of the time elapsed after myocardial infarction, both in the healing and healed phases, on modulation of beat-to-beat ventricular repolarization variability using a multilead criteria. Finally, the best detection of beat-to beat repolarization variability in the anterior group and inferior group, were obtained employing V4 and aVF leads respectively.

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