

Novel technique for ST-T interval characterization in patients with acute myocardial ischemia

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ABSTRACT

Background: The novel signal processing techniques have allowed and improved the use of vectorcardiography (VCG) to diagnose and characterize myocardial ischemia. Herein, we studied vectorcardiographic dynamic changes of ventricular repolarization in 80 patients before (control) and during Percutaneous Transluminal Coronary Angioplasty (PTCA).

Methods: We propose four vectorcardiographic ST-T parameters, i.e., (a) ST Vector Magnitude Area (\mathbf{aST}_{VM}); (b) T-wave Vector Magnitude Area (\mathbf{aT}_{VM}); (c) ST-T Vector Magnitude Difference ($\mathbf{ST-T}_{VD}$), and (d) T-wave Vector Magnitude Difference (\mathbf{T}_{VD}). For comparison, the conventional ST-Change Vector Magnitude (\mathbf{STC}_{VM}) and Spatial Ventricular Gradient (\mathbf{SVG}) were also calculated.

Results: Our results indicate that several vectorcardiographic parameters show significant differences (p -value < 0.05) before starting and during PTCA. Statistical minute-by-minute PTCA comparison against the control situation showed that ischemic monitoring reached a sensitivity=90.5% and a specificity=92.6% at the 5th minute of the PTCA, when \mathbf{aST}_{VM} and $\mathbf{ST-T}_{VD}$ were used as classifiers.

Conclusions: We conclude that the sensitivity and specificity for acute ischemia monitoring could be increased with the use of only two vectorcardiographic parameters. Hence, the proposed technique based on vectorcardiography could be used in addition to the conventional ST-T analysis for better monitoring of ischemic patients.

1. Introduction

Myocardial ischemia is a cardiac condition characterized by decrease in blood flow due to an obstruction or stenosis of the coronary arteries. If ischemia persists, it may convert into an infarction, event that usually is reflected in the Electrocardiogram (ECG). Moreover, a sudden occlusion in one of the major coronary arteries (in the absence of a coronary collateral flow) results in transmural myocardial ischemia, the first step of the so called ischemic cascade

phenomenon. The chain of events usually proceeds in a sequence, that is ischemia, diastolic dysfunction (poor relaxation), systolic dysfunction (weak contraction), ECG changes (ST-deviation), angina pectoris (brought about by accumulation of metabolites), and finally infarction [1].

Different studies [1] have demonstrated that myocardial ischemia modifies segments and waves of left ventricular depolarization and repolarization (QRS complex and ST-T segment, respectively).

New signal processing techniques have allowed use of the vectorcardiogram (VCG), as derived from the ECG, for detecting cardiac ischemia [2]. Computerized VCG has diverse advantages when compared to conventional ECG analysis, particularly because of better specificity, sensitivity and accuracy for the diagnosis of several cardiac pathologies [3]. Often, the advantage of the VCG lies in the time relations between the leads that remain intact during vector analysis and are lost in separate scalar lead analysis because time delays to the same electrical stimulus are different in each lead.

Several researchers have developed different techniques based on the VCG to study cardiac ischemia. Bortolan et al., for example,

proposed characterizing the VCG with parameters based on the T-wave loop morphology [4,5]. Nowinski et al., in turn, have detected changes in ventricular repolarization during coronary angioplasty observing that the T-loop morphology is more sensitive to coronary occlusion than the QT dispersion [6], while Rubulis et al., from the same research team, used the T-loop morphology rather than the T-vector angle to separate coronary disease patients from healthy subjects [7]. Moreover, in 2010, these same researchers evaluated from 3D vectorcardiography the ST-segment vector magnitude, the T-wave vector angle and the T-wave vector loop morphology at baseline versus maximum ischemia [8]. They analyzed ventricular repolarization changes during coronary occlusion and associated both to the size and location of myocardium at risk, which was estimated by SPECT (Single Photon Emission Computed Tomography).

An alternative vectorcardiographic analysis has been carried out through the study of several indexes, such as the QRS vector difference (QRS_{VD}), ST vector magnitude (ST_{VM}) and ST change vector magnitude (STC_{VM}) [9,11]. Even though these studies do not directly relate to the classical VCG, several researchers have used it to study acute myocardial ischemia and infarction. For example, early continuous QRS_{VD} and STC_{VM} monitoring, in patients with acute ischemic heart disease, may predict the results from an exercise test offering prognostic information. Furthermore, this VCG monitoring can be used to identify myocardial reperfusion at an early stage and to give valuable prognostic information in patients with unstable angina [9,10]. Moreover, the continuous vectorcardiography (c-VCG) seems to be more efficient than Holter monitoring myocardial ischemia and could have a higher sensitivity [11]. Besides, c-VCG allows monitoring of ischemia over prolonged periods, due to its low computational cost.

The Spatial Ventricular Gradient (SVG) is another conventional parameter that allows the study of cardiac conduction and the ventricular action potential duration heterogeneity [12]. The potential to detected cardiac ischemia of this gradient in addition to ST analysis has been reported by Haar et al. [13].

We have recently proposed two studies that use the combination of some new parameters computed from original VCGs with the alternative vectorcardiographic parameters [14,15]. In the first work [14], we studied a set of QRS-loop parameters and ST_{VM} computed from resting records in order to distinguish ischemic patients diagnosed with Coronary Acute Disease (CAD) from healthy subjects. After a classification process using discriminant analysis, it was concluded that QRS loop parameters combined with ST_{VM} improved the sensitivity and specificity values with respect to those obtained using only the ST_{VM} index. Furthermore, in a second study [15] this analysis was extended using a similar set of QRS loop parameters for myocardial ischemia monitoring. In that paper, it was demonstrated that these parameters combined with the classic STC_{VM} , QRS_{VD} and SVG indexes increase sensitivity and specificity for acute ischemia monitoring.

This paper, instead, proposes a vectorcardiographic analysis of the ventricular repolarization (ST-T interval) to monitor acute

myocardial ischemia. To this end, four vectorcardiographic parameters and two conventional indexes (STC_{VM} and SVG) were computed before and during Percutaneous Transluminal Coronary Angioplasty (PTCA). Since balloon occlusion modifies the morphology of the ST-T interval, we hypothesized that the proposed parameters can be used to characterize and monitor acute myocardial ischemia.

2. Materials

The study group consisted of 80 ischemic patients (50 men, age 56 ± 11 yrs, and 30 women, age 59 ± 12 yrs), from the Charleston Area Medical Center in West Virginia, before angioplasty (STAFFIII study). The study was approved by the local investigational review board, and informed consent was obtained from each patient before enrollment. Clinical characteristics of all patients and treated vessel subgroups, which were comparable, are presented in Table 1. The following inclusion criteria had to be met for the study population: no clinical or ECG evidence of intraventricular conduction delay with QRS duration ≥ 120 ms [including left bundle branch block (LBBB) and right bundle branch block (RBBB)], no pacemaker rhythm, atrial fibrillation or flutter, or any ventricular rhythm at inclusion (or during the PTCA). If a patient received more than one balloon inflation during the same procedure, only the first inflation was considered.

Nine standard leads (V1–V6, I, II, III) were recorded in the study using a Siemens-Elena AB (Solna, Sweden), digitized at a sampling rate of 1000 Hz and $0.6 \mu V$ amplitude resolution. Synthesized orthogonal X, Y and Z leads were obtained by the Kors transform [16]. A recent study has demonstrated that Kors synthesis matrix provides a better estimation of Frank leads than the Inverse Dower transform [17].

3. Methods

Fig. 1 illustrates a block diagram of the different stages of the analysis. They are explained in the following subsections.

3.1. Preprocessing

In order to reduce low and high frequency noise, all ECG records were preprocessed with a band-pass filter (Butterworth: 4th order, 0.2–100 Hz, and bidirectional). To minimize power-line

Table 1
Clinical characteristics of the 80 studied patients subdivided according to the treated vessel, Left Anterior Descending Artery (LAD), Left Circumflex Artery (LCx) and Right Coronary Artery (RCA).

	All(n=80)	LAD(n=28)	LCx(n=17)	RCA(n=35)
Age (years)	57 \pm 11	59 \pm 12	59 \pm 14	55 \pm 9
Male	50	15	11	24
Number of treated vessels				
1 vessels	73	27	12	34
2 vessels	7	1	5	1
PTCA occlusion time (min)	4.3 \pm 1.3	3.7 \pm 1.2	4.7 \pm 0.7	4.5 \pm 1.5

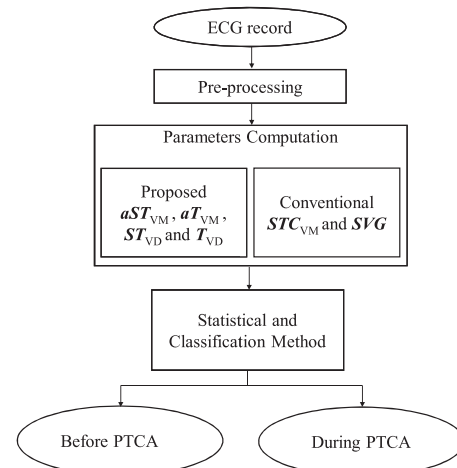


Fig. 1. Proposed analysis general diagram.

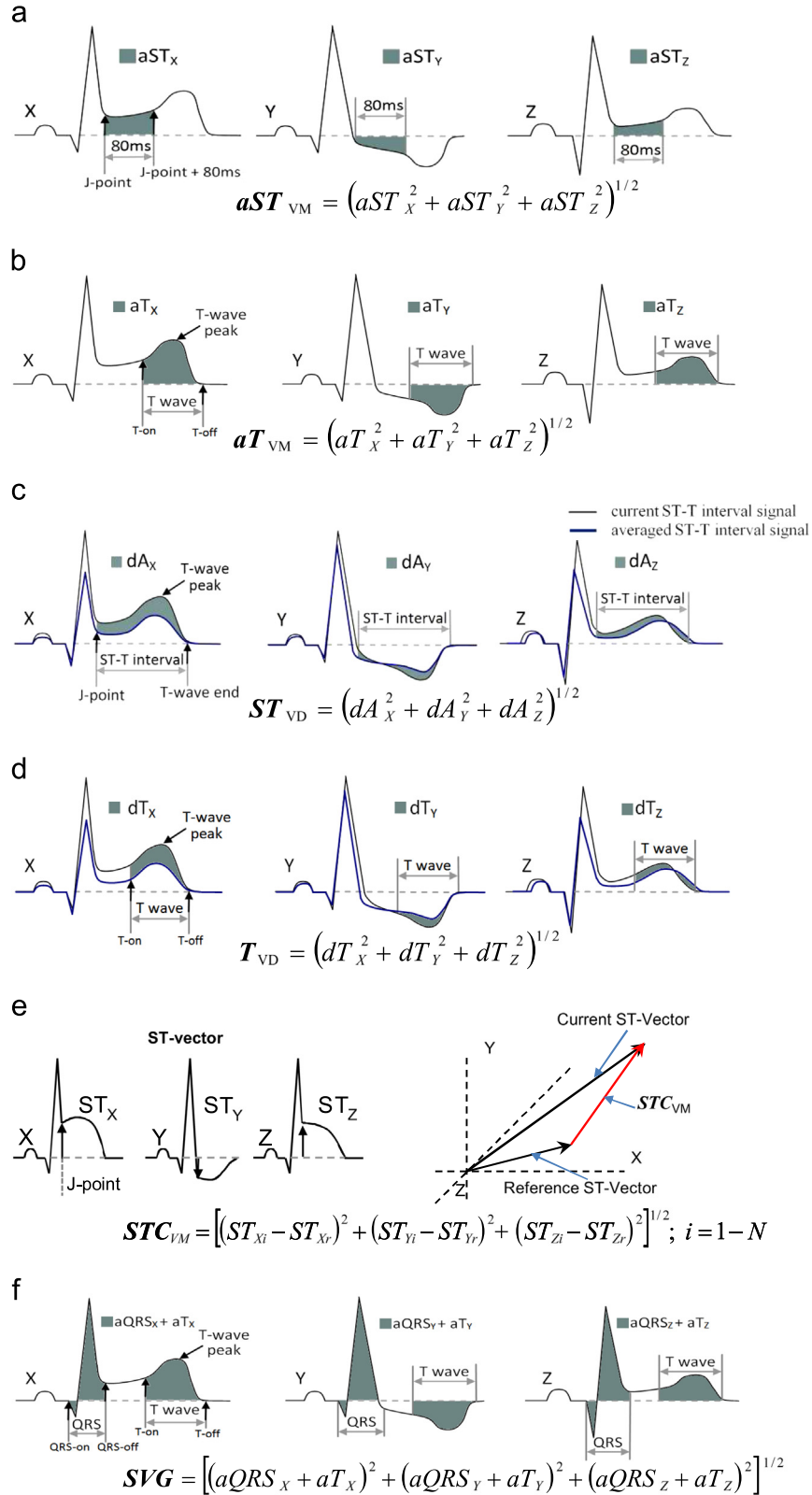


Fig. 2. Vectorcardiographic parameters computation.

interference, a notch filter (Butterworth: 2th order, 50/60 Hz, and bidirectional) was used. Besides, a cubic spline interpolation filter was employed to attenuate ECG baseline drifts and respiratory artifacts. The QRS-complex, T-wave and their endpoints were detected in each ECG using a wavelet-based technique [18]. Excessively noisy beats (with a RMS noise level > 40 μ V,

measured within a 40 ms window located at 2/3 of the RR interval) were excluded. In addition, with the use of a cross-correlation technique, ectopic beats were eliminated by comparing incoming signals against a previously established template. A visually low-noise normal beat extracted from the ECG record was selected as template (or reference) beat, as proposed in [19].

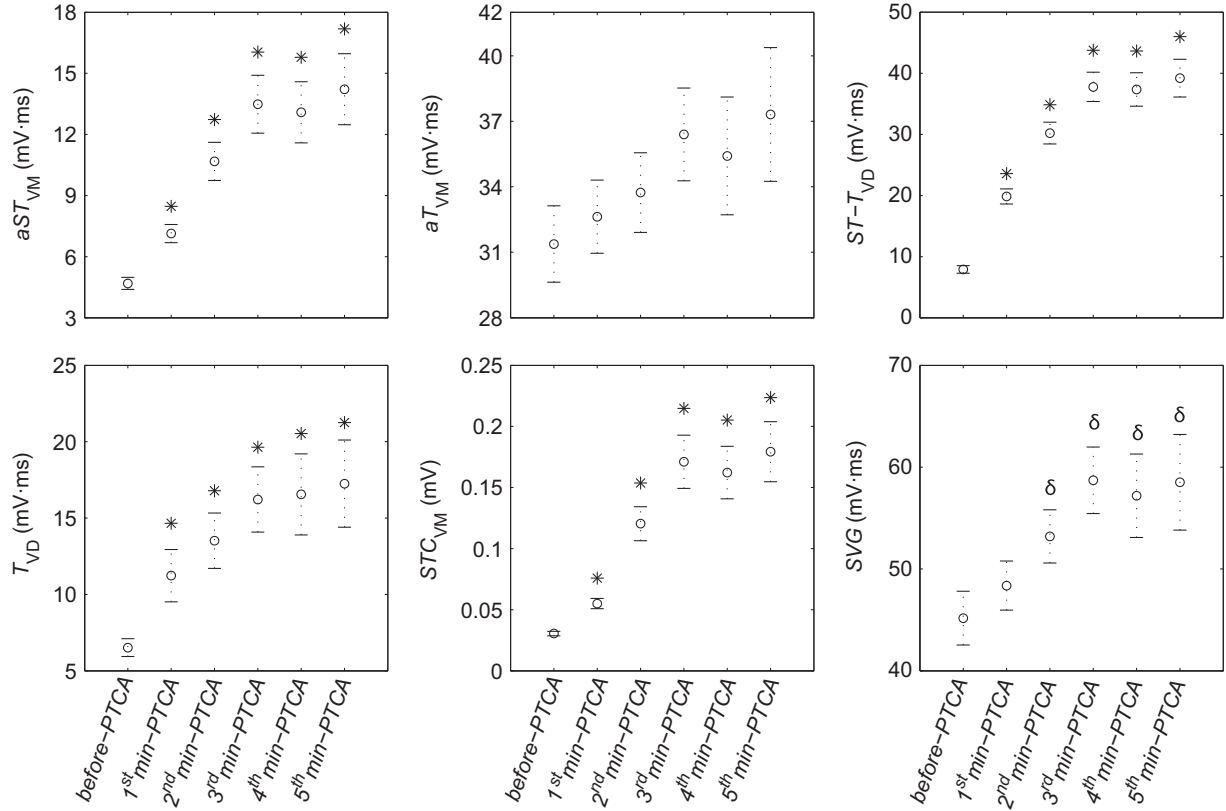


Fig. 3. Mean and standard error of the mean of each parameter computed before starting and during PTCA (the latter parameters were grouped at intervals of 1 min, thereby obtaining 5 groups for each record). * and δ denote statistical significance, p -value < 0.0001 and p -value < 0.05 , respectively (see Section 3.3).

3.2. Parameters computation

Four vectorcardiographic parameters were computed from the ST-T interval for each detected beat. For comparison, the conventional \mathbf{STC}_{VM} and the \mathbf{SVG} were also computed.

ST Vector Magnitude Area ($a\mathbf{ST}_{VM}$), defined as the magnitude of the vector composed of the X, Y and Z areas between the amplitude of the ECG signal interval from each J-point to J-point+80 ms (ST-segment) and the isoelectric level, that is as follows:

$$a\mathbf{ST}_{VM} = (a\mathbf{ST}_X^2 + a\mathbf{ST}_Y^2 + a\mathbf{ST}_Z^2)^{1/2} \quad (1)$$

This index represents the isoelectric level changes between the end of depolarization to the beginning of repolarization.

This parameter is a modification of the \mathbf{STC}_{VM} widely used in the monitoring of cardiac ischemia [9–11]. The principal difference between the two indexes is that \mathbf{STC}_{VM} is evaluated at one point on the ECG (usually J-point, or J-point+60 ms), and in contrast, the proposed $a\mathbf{ST}_{VM}$ is computed during all ST segment (Fig. 2a).

T-Vector Magnitude Area ($a\mathbf{T}_{VM}$), defined as the magnitude of the vector composed of the X, Y and Z areas between the amplitude of each T-wave and the isoelectric level (Fig. 2b), that is

$$a\mathbf{T}_{VM} = (a\mathbf{T}_X^2 + a\mathbf{T}_Y^2 + a\mathbf{T}_Z^2)^{1/2} \quad (2)$$

This index evaluates the T-wave changes, i.e., the transmural and apex-base myocardial recovery.

ST-T Vector Difference ($\mathbf{ST-T}_{VD}$), defined as the difference in area between the ST-T interval (from the J-point to the T-wave end) and the reference of the ECG (at ST-T) evaluated at the first 30 s of each record, that is

$$\mathbf{ST-T}_{VD} = (d\mathbf{A}_X^2 + d\mathbf{A}_Y^2 + d\mathbf{A}_Z^2)^{1/2} \quad (3)$$

The objective of this parameter is to estimate all changes produced during left ventricular repolarization (Fig. 2c).

T-Vector Difference (\mathbf{T}_{VD}), defined as the difference area between the ECG signal at the current T-wave interval and the reference (T-wave interval), evaluated during the first 30 s of each record, that is

$$\mathbf{T}_{VD} = (dT_X^2 + dT_Y^2 + dT_Z^2)^{1/2} \quad (4)$$

This parameter aims at estimating changes produced in the T-wave (Fig. 2d).

ST-Change Vector Magnitude (\mathbf{STC}_{VM}), the ST-vector is composed of the (X, Y and Z) ST-segment deviations from the isoelectric level, measured as the ECG amplitude at the J-point (Fig. 2e); it is a widely used parameter when monitoring cardiac ischemia [9–11]. This vector is the difference between the ST-vector of the current beat and the averaged beat evaluated at the first 30 s of each record, that is

$$\mathbf{STC}_{VMi} = [(ST_{Xi} - ST_{Xr})^2 + (ST_{Yi} - ST_{Yr})^2 + (ST_{Zi} - ST_{Zr})^2]^{1/2} \quad (5)$$

where r denotes the reference beat, i is the current beat, with $i=1, \dots, N$, and N stands for the total number of analyzed beats (Fig. 2e).

Spatial Ventricular Gradient (SVG), defined as the vector QRS-T interval, that is

$$\mathbf{SVG} = [(a\mathbf{QRS}_X + a\mathbf{T}_X)^2 + (a\mathbf{QRS}_Y + a\mathbf{T}_Y)^2 + (a\mathbf{QRS}_Z + a\mathbf{T}_Z)^2]^{1/2} \quad (6)$$

where $a\mathbf{QRS}_X$, $a\mathbf{QRS}_Y$, $a\mathbf{QRS}_Z$ and $a\mathbf{T}_X$, $a\mathbf{T}_Y$, $a\mathbf{T}_Z$ are the QRS-complexes and T-wave areas on the orthogonal leads, respectively, and all expressed in mV and ms. Thus, \mathbf{SVG} carries the same units. Unlike most other ECG parameters, the \mathbf{SVG} is not influenced by changes in ventricular conduction; it only changes if the distributions of either the ventricular action potential morphology and/or duration are altered [12] (Fig. 2f).

Fig. 2 shows the computation of each parameter and the two conventional indexes.

Table 2

Classification outcomes for each computed index and for the best combination of them.

	aST_{VM}		aT_{VM}		ST-T_{VD}		T_{VD}		STC_{VM}		SVG		aST_{VM} and ST-T_{VD}	
	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec	Sens	Spec
1 st min	68.08	66.25	41.42	54.83	74.21	84.08	58.58	82.12	71.54	64.71	48.38	59.33	78.37	82.00
2 nd min	74.25	71.29	49.13	48.00	88.75	88.92	71.50	81.12	71.21	90.96	53.71	62.04	87.38	90.04
3 rd min	74.95	78.21	47.71	61.83	88.57	91.75	78.24	83.29	75.76	88.04	60.62	66.13	87.43	94.00
4 th min	74.25	75.50	51.13	49.46	86.56	92.12	77.19	83.79	77.31	82.50	55.88	67.54	87.13	91.71
5 th min	72.13	75.88	55.67	47.50	91.00	92.13	81.27	85.54	80.80	86.71	54.60	68.58	90.53	92.58

Table 3

Classification results for the best combination of the computed index and each treated vessel.

	LAD (n=28)		LCx (n=17)		RCA (n=35)	
	Sens	Spec	Sens	Spec	Sens	Spec
1 st min	86.00	84.08	80.80	84.71	78.80	73.17
2 nd min	95.88	95.46	83.80	94.54	83.40	87.29
3 rd min	94.43	95.92	89.00	90.67	87.56	88.42
4 th min	93.75	96.75	89.25	93.37	86.00	87.33
5 th min	90.67	95.50	90.75	93.62	88.86	91.50

3.3. Statistical and classification methods

The parameters described above were computed for each detected sinus beat in every ECG record. In order to quantify the discrepancy between the parameters' distribution and the Gaussian distribution, we analyzed the normality of these values using the D'Agostino–Pearson test [20]. It has been observed that the underlying variables' distribution is non-Gaussian. Comparisons between each parameter mean value computed before starting and during episodes of PTCA (the last one grouped at 1 min intervals) were made using the non-parametric Mann–Whitney test.

Thereafter, the mean value of each parameter along the entire record was calculated. Such features were used as inputs to a classifier based on Linear Discriminant Analysis (LDA) [21] with the aim of distinguishing (or separating out) ischemic patients before starting PTCA for the same patients during each minute of the PTCA procedure.

The resulting discriminant function can be used to assign each record to a particular group or class (in this case, before starting or during PTCA), based on its values of discriminate variables. The model coefficients are estimated with a subset of ECG records for which the group is known. This subset of observations is sometimes referred to as the *training subset* (we used 70% of the records).

To validate the model, this discriminant function was used to predict the group of another different subset (referred to as *validation subset*), making use of the remaining 30% of the records. Since these outcomes depend on the records chosen for the training and validation stages, we randomly selected 100 different training and validation subsets to improve the statistical reliability of the results. With such subsets, 100 different discriminant functions were computed.

In order to study the variation of the proposed parameters according to the ischemic cardiac area, the described classifier was also evaluated in each set of patients grouped by the treated artery (LAD, LCx or RCA). To evaluate the LDA classifier performance, the Receiver Operating Characteristic (ROC) curve was computed. The optimal cut-off point in the ROC on that curve was determined as the point that maximizes the Sens and Spec sum (assumed that the 'cost' of a *false negative* result is the same as that of a *false positive* one [22]). Finally, the global performance of the classifier was evaluated with the Area Under the ROC Curve (AUC).

4. Results

Four vectorcardiographic parameters were evaluated on the XYZ orthogonal leads. Fig. 3 shows the Mean and Standard Error of the Mean (SEM) values computed for each parameter before starting and during episodes of PTCA. To follow up the evolution of each parameter during PTCA, we grouped the values during balloon occlusion at intervals of 1 min, thereby obtaining 5 groups for each record. Values marked with * and δ indicate the statistical significance (p -value < 0.0001 and p -value < 0.05 respectively) between before and during PTCA.

On the basis of the statistical analysis (see Section 3.3), Fig. 3 shows that all the vectorcardiographic parameters (with the exception of the **aT_{VM}** for all min and the **SVG** at the 1st minute during PTCA) produced significant differences (p -value < 0.05) before starting and during episodes of PTCA.

The mean values of the classification results are shown in Table 2, where the Sens and Spec values are displayed for different classification schemes using

- individual index (proposed and conventional), to study the discrimination ability,
- the best combination of the parameters (say **aST_{VM}** and **ST-T_{VD}**). This pair was obtained by Wilks' lambda technique, which evaluates the correlation intra- and inter-group to find the parameters combination with the best discriminating capacity.

Table 3 displays the mean values of the classification results for each set of coronary vessels (LAD, LCx or RCA) using only the best combination of parameters (**aST_{VM}** and **ST-T_{VD}**).

It can be seen that in every treated vessel the lowest classification values were obtained at the start of the PTCA. Moreover, the best performance values occurred at different times: the 2nd minute during angioplasty for the LAD set and close to the end for the LCx and RCA groups.

Fig. 4 shows the ROCs Curves and their corresponding areas, for the classification schemes using the best combination of parameters (**aST_{VM}** and **ST-T_{VD}**) for each 1 min interval during PTCA.

5. Discussion and conclusions

The hypoxia caused by myocardial ischemia leads to a depletion of ATP cellular stores and subsequent electromechanical dissociation. This, in turn, causes changes in the ATP-dependent transmembrane potential that manifest itself as ECG repolarization changes in the ST segment and T wave [1]. In recent years, many researchers have proposed algorithms for studying myocardial ischemia using electrocardiographic and vectorcardiographic techniques. Most of these algorithms are based on cardiac repolarization shape, reflected in the ECG by the ST-segment, ST-T interval and T-wave, and in the VCG via the T-wave loop and the computation of **SVG**, **ST_{VM}** and **STC_{VM}** indexes. Using this approach,

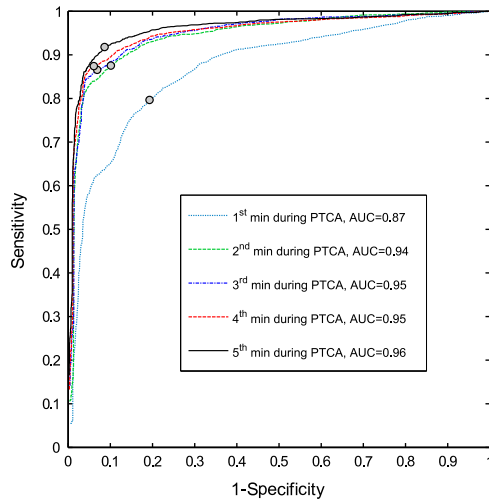


Fig. 4. ROC curves and their corresponding Area Under these Curves (AUC), for the classification schemes using the aST_{VM} and $ST-T_{VD}$ combination.

Manocha and Singh [23] summarized most of the ECG techniques and concluded that the sensitivity and positive predictability of the ST-segment lead to an average value of 87–89% and 90–92%, respectively. However, unlike our work, most techniques in this overview have been evaluated using the MIT/BIH European ST-T database. Thus, although these results may not be directly compared with those obtained in our study, they do give an idea of the sensitivity of the ST segment detection techniques, which are lower than those shown in our work. Furthermore, most of these techniques are based on the standard 12-lead ECG analysis, which increased the computational cost. In contrast the VCG analysis only required XYZ-lead ECG which reduces the computational cost and allows on line monitoring.

Furthermore, a review has demonstrated the superiority of VCG-based techniques versus those based on ECG alone; vectorcardiography provides a better and more rational insight into the electrical phenomena that occur spatially [3]. Moreover, in [24], Jensen et al. compared on-line computerized VCGs derived from 12-lead ECGs, and concluded that the first one is a more sensitive method for detecting myocardial ischemia during coronary angioplasty. However, most of those studies based on VCG analysis use the STC_{VM} and SVG parameters.

In order to further describe cardiac ischemic changes we propose four vectorcardiographic parameters, calculated from the ST-T segment (aST_{VM} , aT_{VM} , $ST-T_{VD}$ and T_{VD}). These were compared with the conventional indexes mentioned above.

Moreover, the proposed parameters, similar to conventional indexes, tend to gradually increase their mean values as angioplasty occlusion persists over time. Simultaneously, ischemia worsens the changes in cardiac repolarization, indicating a direct relationship with our parameters. These findings could be used in a combined analysis to improve monitoring of acute myocardial ischemia.

Discriminant analysis (Table 2) indicates that the vectorcardiographic parameter with the best global performance was $ST-T_{VD}$, which reached a $Sen=91.0\%$ and a $Spec=92.1\%$. Furthermore, the minute-by-minute statistical comparison led to an acute ischemic monitoring greatly enhanced when the parameters $ST-T_{VD}$ and aST_{VD} were used, reaching a $Sens=90.5\%$ and a $Spec=92.6\%$ at the 5th minute of the PTCA.

In addition, when we compared the minute-by-minute $Sens$ and $Spec$ values obtained with the standard monitoring parameters (STC_{VM} and SVG) with those obtained with the best combination of the proposed parameters, we can see that the latter are higher throughout the occlusion. Moreover, each

parameter increased their Sen and $Spec$ values during the PTCA, clearly showing the close relation between the parameters and the ischemic condition. Hence, it can be inferred that the increase in performance of the classifier, when angioplasty occlusion persists in time, is due to the cardiac repolarization aggravation caused by the sustained ischemia.

However, some patients were not included in all the analyses (1 min, 2 min, ... 5 min) because duration of the PTCA procedure was different and, in some cases, less than 5 min. Thus, for the analysis of the 1st and 2nd minute of the occlusion, all ECG records were used, while for the 3rd, 4th and 5th minute we used only 71, 55 and 50 ECG recording, respectively.

Our findings are supported by those from Fayn et al. [25], which were compared to conventional ST segment criteria [26], using the same database. Although, the used technique has an excellent performance in ischemia detection, the authors do not report findings regarding myocardial ischemia monitoring. Therefore, the results obtained with our technique are better than those achieved with the ST segment standard criteria (they reached values of $Sens=60\%$ and $Spec=88\%$) and comparable with those obtained by other researchers using the same database.

As for the values of Sen and $Spec$ shown in Table 3, it should be underlined that

- (a) they tend to decrease in patients who underwent angioplasty in the RCA;
- (b) they are significantly higher in the group of patients with a treated LAD; and
- (c) they are similar to the group of patients with a treated LCx.

All of the above is said with respect to the values obtained for the entire population shown in Table 2. It is necessary to highlight that the proposed parameters permit classifying up to $Sens=90.7\%$ and $Spec=93.6\%$ in patients who underwent angioplasty in the LCx (always relative to the reference situation). Other authors have reported that the sensitivity of conventional vectorcardiographic parameters (ST_{VM} and STC_{VM}) for detecting cardiac ischemia based on the treated vessel decreases from LAD to RCA to LCx. [27]. This implies that our technique can provide additional information in monitoring patients with compromised LCx artery, currently not available with the standard ST analysis.

Finally, the best AUC value (Fig. 4), using aST_{VM} and $ST-T_{VD}$ is 0.96, after the 5th minute of the balloon inflation. Thus, it indicates high effectiveness for the proposed classification technique. This AUC value is considered of high accuracy in diagnostic tests [28].

Only 17 patients out of the 80 comprising the studied group had a compromised LCx artery. Such a small number is perhaps a limitation. Nevertheless, it should be necessary to evaluate the proposed technique in more patients to improve the accuracy of the $Sens$ and $Spec$ values.

In conclusion: the proposed vectorcardiographic technique study could be used in addition to conventional ST-T analysis for better monitoring of ischemic patients. From the clinical point of view, the most important future application would be the ambulatory monitoring of ischemic patients in Holter or stress tests studies.

Conflict of interest statement

None declared.

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