Morphologic Features of the ECG for Detection of Stress-Induced Ischemia

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Abstract

In this work we evaluated the improvement in the detection of stress induced ischemia achieved by ECG features not commonly measured by cardiologists. We evaluated 927 patients recorded during treadmill exercise SPECT following the Bruce protocol. The patients were labeled in three groups by two experts according to their SPECT images as: no ischemia (Ischemic Miocardium (IM)$< 5\%$), mild ischemia ($5\% \leq$IM$< 10\%$) and moderate/severe ischemia (IM$\geq 10\%$). The features studied were grouped as pretest features, exercise features and those proposed in this work. Among the features proposed, we included the Q, R, and S wave amplitudes, the slopes around each wave, and estimates of the P and T wave widths, as well as the QRS complex width. We also studied other features related to the ST segment. For the detection task, we used logistic regression, while the performance was evaluated using k-fold crossvalidation. Most discriminant features were selected using a feature selection algorithm for two thresholds of ischemia, $\geq 5\%$ and $\geq 10\%$. Finally, two models of features were evaluated and compared to those reported by Sharir et al. obtaining improved performance for $\mathrm{IM} \geq 5\%$ *in Se 77%, Sp 88% and AUC 0.88; while for* $\mathrm{IM} \geq 10\%$*, Se 76%, Sp 90% and AUC 0.95.*

1. Introduction

The analysis of the electrocardiogram (ECG) during exercise stress testing (EST) was first used by Feil and Siegel in 1928 [1]. Nowadays this technique is widely used as the first test for detecting coronary artery disease (CAD). In this preliminary study we evaluated unconventional and well established features measured on the ECG for detecting stress-induced ischemia. Some of proposed features have proven utility in the field of heartbeat classification [2], while others, despite well documented [3], never were studied in a large cohort of patients. In recent years features measured in the QRS complex such as slopes or high frequency components (HFQRS) were studied and compared [4, 5]. The recent availability of ECG data recorded in a large cohort of consecutive patients undergoing stress test, as well as myocardial perfusion images (MPI) serving as gold standard, provide an adequate framework for the development of improved ischemia detectors based on ECG measurements [5, 6]. The aim of this study was to compare the diagnostic performance and incremental value in detecting exercise-induced ischemia, using several unconventional features extracted from the ECG and MPI as a gold standard.

2. Material and methods

In this work we used the database "Exercise testing and perfusion imaging" distributed by [6] and previously described in detail [5]. The database includes 927 patients referred for exercise MPI single photon emission computed tomography (SPECT). During the test, 12-lead ECG was recorded until the recovery phase at a sampling rate of 1000 Hz, 0.15 μV of resolution and an analog bandwidth from 0.05 to 125 Hz. Perfusion images were visually analyzed by two experts and the amount of ischemic myocardium (IM) was calculated as the summed difference score between stress and rest scores. Finally patients were labeled as: no ischemia or equivocal (IM$< 5\%$), mild ischemia ($5\% \leq$IM$< 10\%$) and moderate/severe ischemia (IM$\geq 10\%$). From the 927 patients available, 18 were discarded due to missing clinical or MPI data or bad quality ECG recording. A summary of the clinical characteristics is shown in Table 1 (a more complete description can be found in [5]).

The first stage for ECG noise reduction was to low-pass filter (FIR, $fc = 35$ Hz, 80 db stop) in order to suppress power-line and high frequency noise. Next, QRS complex detection was performed with a validated algorithm [7]. The fiducial points previously obtained are used to calculate a signal-averaged heartbeat (SAHB) with all normal

Table 1. Scheme of the division and clinical characteristics.

	Myocardial Ischemia			
	None	Mild	Severe	All
#	843	32	34	909
IM (%)	0 ± 0.3	7 ± 1	17 ± 6	1 ± 4
Age	55 ± 10	61 ± 11	59 ± 11	55 ± 10

heartbeats in the previous 20 seconds, thus attenuating part of the noise not synchronized with the heartbeats. This SAHB is calculated at rest, at peak exercise (PE or max HR) and after peak exercise (AP), i.e. when the HR is below 128 bpm, to avoid T and P waves to overlap. All features were calculated either in the SAHB, or in the wavelet transform (WT) of the SAHB. The prototype wavelet used is the as in [2].

The features used can be grouped in three categories: 1) pretest, or those calculated before the EST, 2) exercise, or those typically measured in EST and 3) those proposed in this work. These features are summarized in Table 2. The features proposed in this study were calculated in two modalities: 1) as a ratio, relative to the value of the feature at rest, e.g. the value is 1 if no change, and 2) as two features, one value at rest and other at either PE or AP, in case the absolute value retains discriminant information. Also the feature measurements along ECG leads are integrated according to: 1) calculating features in the first two principal components (PCA1 and 2) [8], and 2) calculating the feature for each lead, and then mapping each feature value to the $[0,\ 1]$ domain with a logistic function $\frac{1}{1+e^{-x}}$. Then values from the 12 leads are summed into the final feature value in the $[0,\ 12]$ domain. We referred to this strategy as soft integration (SFT).

In [2] we used feature k_Z^{QRS} as a robust surrogate of QRS complex width. We extrapolated this concept to the P wave, and ST-T complex by moving the analysis window to $\mathrm{QRS_{on}} - [200,\ 50]$ ms and $\mathrm{QRS_{off}} + [0,\ 350]$ ms positions respectively. The slopes of the QRS complex were studied in [4], and performed better than HFQRS in detecting acute myocardial ischemia during PTCA. As the analog bandwidth of the recordings has a cut off in 125 Hz, HFQRS features calculated in [5] could not be studied here. However, r^{WTx} measures the higher frequency band of QRS complex, given the bandpass nature of the WT. The rest of the features enumerated in Table 2 are described in [3], but are not conventionally used in EST.

The feature vector $\mathbf{x}$ is constructed with the values described above, followed with a 1. Then $\mathbf{x}$ was used with a logistic regression detector

$$p(\mathbf{x}) = \frac{1}{1 + \mathrm{e}^{-\mathbf{a}^{\mathbf{T}}\mathbf{x}}} \tag{1}$$

where the patient is classified as ischemic if $p(\mathbf{x}) > 0.5$. The process of training the detector consists in estimating the vector of regression coefficients $\mathbf{a}$ with an iterative algorithm, while the evaluation in calculating $p(\mathbf{x})$. The implementation of the detector was performed using the PRTools toolbox [9].

As one of the objectives of this work was to asses the incremental value of the proposed features with respect to the *a priori* information available, we performed a sequential floating feature selection (SFFS) in three steps [2], one for each group of features in Table 2. Therefore we first performed an SFFS for pretest group, obtain a pretest model and use it as starting point to the following SFFS of exercise features. The same procedure was repeated for the last group of proposed features. This triple-SFFS was repeated for both 5 and 10% IM thresholds, obtaining one final feature model for each. The evaluation of each model within the SFFS was performed following a k-fold cross-validation with $k = 10$ folds. It is important that each cross-validation step implies training in $^{9}/_{10}$ of the database patients, and testing in the remaining $^{1}/_{10}$ of the patients. The optimization parameter for the SFFS is the area under (AUC) the receiver operating curve (ROC). The two feature models obtained were finally evaluated in the whole database, as performed in [5].

3. Results

The models obtained from the SFFS are presented in Table 3. The group of proposed features selected for $\mathrm{IM} \geq 5\%$ were: 1) features from Q and R waves amplitudes, 2) all slopes of the QRS complex, 3) features related to the QRS complex width measured at WT scales 3 and 4, 4) features related to the duration of ventricular repolarization at WT scales 3 and 4, 5) the energy of the QRS complex measured at WT scales 3 and 4 and 6) the ST normalized by the R wave amplitude after PE. The final evaluation resulted for the threshold of $\mathrm{IM} \geq 5\%$, in a sensitivity (Se) of 77%, specificity (Sp) of 88% and AUC of 0.88, while for $\mathrm{IM} \geq 10\%$, Se 76%, Sp 90% and AUC 0.95. These results are presented in Table 4 and compared with the results obtained in [5]. Figure 1 shows the incremental value of the proposed features as they are included into the model.

4. Discussion and conclusions

In this work we presented a model of features for ischemia detection in EST, based on three groups: pretest, exercise and a set of proposed measurements calculated in ECG recordings of conventional analog bandwidth. The proposed group of features is the main methodological contribution with respect to [5]. These features were calculated in most of the cardiac cycle in order to measure the effect of stress-induced ischemia. Some of the fea-

Table 2. Features used in this work.

Group	Feature	Description
Pretest	Pretest score – Age – Gender – Infarction – Smoking – Lipids – Diabetes – STT changes – Max age-pred HR – Systolic BP – Diastolic BP	Clinical features included with the database. Description available in [6]. BP at rest
Exercise	EST stage – Max HR – Rest HR – EST duration – HR recovery – HR change – Duke T. score – Chest Pain – Systolic BP PE – Diastolic BP PE	EST duration in seconds. Chest pain: typical - atypical - none. Exercise features included with the database. Description available in [6].
Proposed	QRS width – $\mathrm{ST}_{\mathrm{PE}}$ – $\mathrm{ST}_{\mathrm{AP}}$ – $(\mathrm{ST}/\mathrm{R})_{\mathrm{PE}}$ – $(\mathrm{ST}/\mathrm{R})_{\mathrm{AP}}$ – $\mathrm{ST}_{\mathrm{PE}}/\mathrm{RR}_{\mathrm{PE}}$ – $x(k_{\mathrm{Q}})$ – $x(k_{\mathrm{R}})$ – $x(k_{\mathrm{S}})$ – s_{Q}^{-} – $s_{\mathrm{R}}^{\mathrm{Q}}$ – $s_{\mathrm{S}}^{\mathrm{R}}$ – s_{-}^{S} – k_Z^P – k_Z^{QRS} – $k_Z^{\mathrm{ST-T}}$ – r^{WTx} – t_{r50}	RT: rest. PE: peak exercise. AP: After PE. ST/R ST normalized with respect R wave [3]. $x(k_{\mathrm{X}})$ ECG value at X wave. $s_{\mathrm{Y}}^{\mathrm{X}}$ slope between X and Y waves. k_Z^{X} zero-cross position of the WT autocorrelation signal in P, QRS and ST-T [2]. r^{WTx} RMS calculated in the WT of the QRS complex at scale x. t_{r50} is the time to decrease 50% of the HR change from PE.

Table 3. Features obtained from the SFFS.

IM	Features
$\geq 5\%$	$x(k_{\mathrm{Q}})_{\mathrm{SFT}}$ – $x(k_{\mathrm{Q}})_{\mathrm{PCA2}}^{\mathrm{PE}}$ – $x(k_{\mathrm{R}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $x(k_{\mathrm{S}})_{\mathrm{PCA2}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{PCA2}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{SFT}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{PCA1}}^{\mathrm{PE}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{PCA2}}^{\mathrm{PE}}$ – $(s_{\mathrm{R}}^{\mathrm{Q}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $(s_{\mathrm{S}}^{\mathrm{R}})_{\mathrm{PCA1}}^{\mathrm{RT}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{PCA2}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{PCA2}}^{\mathrm{PE}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $(k_Z^{\mathrm{QRS}})_{\mathrm{PCA2}}^{\mathrm{WT3}}$ – $(k_Z^{\mathrm{QRS}})_{\mathrm{PCA2}}^{\mathrm{WT3-PE}}$ – $(k_Z^{\mathrm{QRS}})_{\mathrm{PCA2}}^{\mathrm{WT4-PE}}$ – $(k_Z^{\mathrm{QRS}})_{\mathrm{SFT}}^{\mathrm{WT3}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA1}}^{\mathrm{WT3-PE}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA1}}^{\mathrm{WT3-RT}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA2}}^{\mathrm{WT3-PE}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{SFT}}^{\mathrm{WT3-PE}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{SFT}}^{\mathrm{WT4}}$ – $r_{\mathrm{PCA1}}^{\mathrm{WT4}}$ – $r_{\mathrm{SFT}}^{\mathrm{WT3-RT}}$ – $r_{\mathrm{PCA1}}^{\mathrm{WT4-PE}}$ – $r_{\mathrm{PCA1}}^{\mathrm{WT4-RT}}$ – $(\mathrm{ST}/\mathrm{R})_{\mathrm{AP}}$ – EST stage – Max HR – Rest HR – Duke T. score – Atypical EST induced CP – Age – Gender – Infarction – Max age-pred HR – Systolic BP RT
$\geq 10\%$	$x(k_{\mathrm{Q}})_{\mathrm{PCA1}}^{\mathrm{RT}}$ – $x(k_{\mathrm{R}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $x(k_{\mathrm{R}})_{\mathrm{SFT}}^{\mathrm{PE}}$ – $x(k_{\mathrm{S}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $x(k_{\mathrm{S}})_{\mathrm{PCA2}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{PCA1}}^{\mathrm{RT}}$ – $(s_{\mathrm{Q}}^{-})_{\mathrm{SFT}}^{\mathrm{PE}}$ – $(s_{\mathrm{R}}^{\mathrm{Q}})_{\mathrm{SFT}}^{\mathrm{PE}}$ – $(s_{\mathrm{R}}^{\mathrm{Q}})_{\mathrm{SFT}}^{\mathrm{RT}}$ – $(s_{\mathrm{S}}^{\mathrm{R}})_{\mathrm{PCA1}}^{\mathrm{PE}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{PCA1}}^{\mathrm{PE}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{PCA2}}^{\mathrm{PE}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{PCA2}}$ – $(s_{-}^{\mathrm{S}})_{\mathrm{SFT}}$ – $(k_Z^{\mathrm{P}})_{\mathrm{SFT}}^{\mathrm{WT3-RT}}$ – $(k_Z^{\mathrm{QRS}})_{\mathrm{PCA2}}^{\mathrm{WT4-RT}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA2}}^{\mathrm{WT3}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA2}}^{\mathrm{WT3-PE}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{PCA2}}^{\mathrm{WT3-RT}}$ – $(k_Z^{\mathrm{STT}})_{\mathrm{SFT}}^{\mathrm{WT3-PE}}$ –$(k_Z^{\mathrm{STT}})_{\mathrm{PCA2}}^{\mathrm{WT4-RT}}$ – $r_{\mathrm{PCA1}}^{\mathrm{WT3}}$ – t_{r50} – ST PE – $(\mathrm{ST}/\mathrm{RR})_{\mathrm{SFT}}^{\mathrm{PE}}$ – EST stage – Max HR – Non CP induced EST – Typical CP induced EST – Systolic BP PE – Diastolic BP PE – Pretest Score – Max age-pred HR – Systolic BP RT

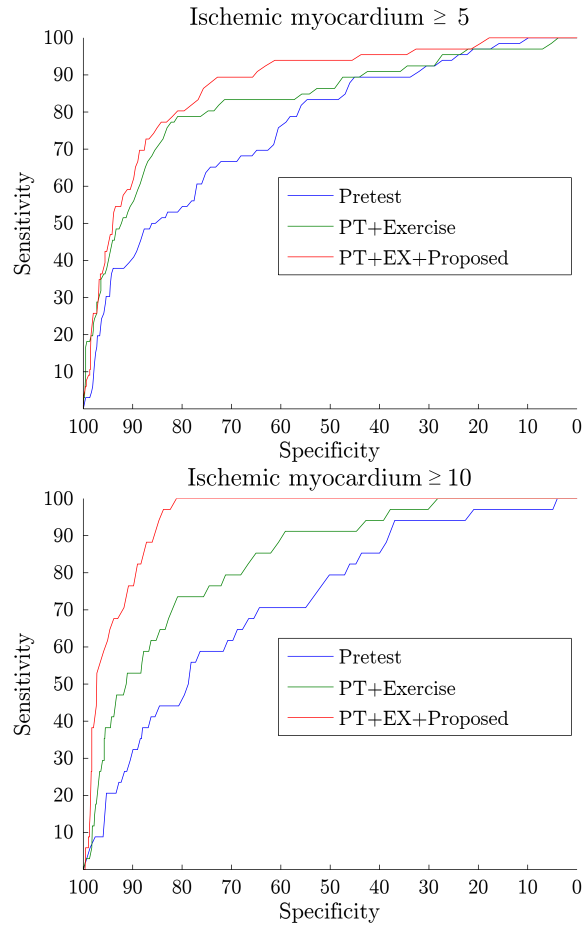

Figure 1. ROC curves for the models shown in Table 3.

Table 4. Final results for the models presented in Table 3.

IM	Description	Se	Sp	AUC	Comment
$\geq 5\%$	this work	77	84	0.88	crossval.
		86	84	0.92	biased
	Sharir et al. [5]	–	–	–	biased
$\geq 10\%$	this work	76	90	0.95	crossval.
		100	91	0.99	biased
	Sharir et al. [5]	88	78	0.89	biased

tures were studied in previous works in the context of ischemia detection [3, 4], while others as k_Z^{X} were successfully used for heartbeat classification [2]. The performance improvement of each feature was analyzed with an SFFS algorithm, obtaining two models, one for IM$\geq 5\%$ and the other for IM$\geq 10\%$, which maximized the AUC calculated in a crossvalidated fashion. We chose these evaluation approach to avoid obtaining a model too overfitted to the data, as could happen in [5]. Of the features included in the models, measurements around the Q wave seem to be discriminant ($x(k_{\mathrm{Q}})$, s_{Q}^{-} and $s_{\mathrm{R}}^{\mathrm{Q}}$), this could be related with the fact that the first region affected by ischemia is subendocardial [3]. The terminal slope of the QRS complex (s_{-}^{S}) measured in PCA2 or integrated with the SFT strategy were also included. These features together with those related to the duration of the ventricular repolarization should be further studied to understand its relation with stress-induced ischemia. The duration of the QRS complex (k_Z^{QRS}) is well known to be affected by ischemia, as well as the level of the ST segment [3]. With respect to the high frequency components of the WT QRS complex measured with r^{WTX}, only scales 3 and 4 were included, despite other scales of higher frequency were available for the feature selection. An aspect to be further studied is the importance that each feature has within the model. Respect to the calculation of the features as a ratio respect rest or two separate features, both strategies were selected. As a consequence, further experimentation is required to know which features benefit from each strategy. Finally, it would be interesting to study if features similar to HFQRS, with good performance reported in [5], could contribute to the obtained models. For this purpose we would need ECG recordings with an analog bandwidth up to 250 Hz.

As can be seen in Table 4, the crossvalidated performance is more conservative, but probably more representative of the actual performance of a classifier. According to the ROC curve shown in figure 1, the most challenging detection problem is for IM $\geq 5\%$, for the case of IM $\geq 10\%$ the final model performs extremely well, a symptom that the model could be too overfitted, probably because of the scarcity of severe ischemia patients in the cohort analyzed. However, it is necessary to study how these models performance (and the reported in [5]) generalize to other databases in order to validate the performance improvement presented in this work.

As a result of the methodology presented, the results obtained in Table 4 represent an improvement with respect to those reported in [5].

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