Comparison of ECG-Based Clinical Indexes During Exercise Test

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Abstract

In this work we have compared clinical indexes based on ECG changes found on the ventricular depolarization and repolarization periods in high-resolution exercise test ECGs. Stress echocardiography and coronary angiography were considered as gold standards to label two groups of patients (healthy and ischemic). ST segment deviations and Q, R and S waves amplitudes were automatically measured and included in a multivariate discriminant analysis to automatically classify the patients in the two groups. Results showed that QRS amplitude changes provide a closer description of the heart response to exercise test than ST deviations do (sensitivity/specificity of 79/71% vs. 55/69%, respectively).

1. Introduction

The electrocardiographic signal (ECG) has become the most used non-invasive tool for diagnosis of cardiovascular diseases. Basic and advanced analysis have been applied to the ECG recorded in different situations. One test widely used in the clinical routine is the exercise test, and ST segment deviations are usually measured during exercise.

Other alternative indexes measured on the depolarization period have been recently proposed. The Athens QRS score is defined [1] by the following expression

$$\begin{aligned} QRS &= QRS_{aVF} + QRS_{V5} = \\ &[R-Q-S]_{aVF} - [R'-Q'-S']_{aVF} + \\ &[R-Q-S]_{V5} - [R'-Q'-S']_{V5} \qquad (1) \end{aligned}$$

where R, Q, S represent the respective wave amplitudes during rest, and R', Q', S', the corresponding amplitudes immediately after exercise. The Athens QRS score has been presented as a promising score for detecting coronary artery disease based on exercise induced-changes [1].

In this work we have compared and analyzed ECG changes measuring indexes based both on the ventricular depolarization and repolarization in patients undergoing exercise test. The aim was to provide more insight of variations induced by the exercise and to determine whether changes in QRS amplitudes may better classify patients than ST segment deviations do.

2. Materials and methods

2.1. Study population

A total of 332 ECGs were recorded in patients undergoing exercise test at the "Lozano Blesa" University Hospital, Zaragoza (Spain). The investigation conformed with the principles outlined in the Declaration of Helsinki.

Standard leads (V1, V3-V6, I, II, III, aVR, aVL, and aVF) and lead RV4 (substituting classical V2) were digitally recorded using equipment by Siemens-Elema AB (Solna, Sweden) and sampled at 1 KHz with amplitude resolution of 0.6 μV. The recordings were stored in CD-ROM for further processing.

The gold standards for comparison of stress test-based results were the stress echocardiography and coronary angiography. Those patients with extremely noisy ECG recordings (59), in which the detection algorithms failed, were rejected from the study. The remaining patients were selected and classified into two groups labeled as *ischemic* and *healthy*. We included as *healthy* patients those for whom clinical and electrical stress test results were negative, they were not asked for undergoing echocardiography and reached at least 90% of the maximal (age-related) heart frequency (55 patients); the *ischemic* patients included in the second group were those with positive result either in the stress echocardiography or coronary angiography test (29 patients).

2.2. ECG-based indexes

ST segment deviations

The ST segment level was automatically measured on the ECG signal after signal pre-processing: QRS complexes detection and selection of normal beats, baseline wander attenuation using cubic splines, and rejection of beats presenting differences in their mean isoelectric level with respect to adjacent beats of more than 600 μV). The ST segment level was measured at a HR-dependent distance from the QRS fiducial point according to the expression

$$STpoint = QRS + (40ms + 1.2 \cdot RR_i^{1/2}) \quad (2)$$

and the amplitude at *STpoint* was beat-by-beat estimated with respect to the isoelectric level obtained by averaging 10 ms of signal starting at 80 ms before the QRS fiducial point. This selection based on the QRS fiducial point avoids the always problematic estimation of the J point (especially in noisy ECGs), but considers the effects of the heart rate [2]. The ST segment amplitude was evaluated during the complete stress test procedure for all leads. Filtering was further applied to the trends including a median filter (5 samples) to remove outlier values, and a moving average filter (10 samples) to reduce the noise in the estimation. An example of the filtered ST level trend for lead V3 along a complete exercise ECG recording is shown in Fig. 1.

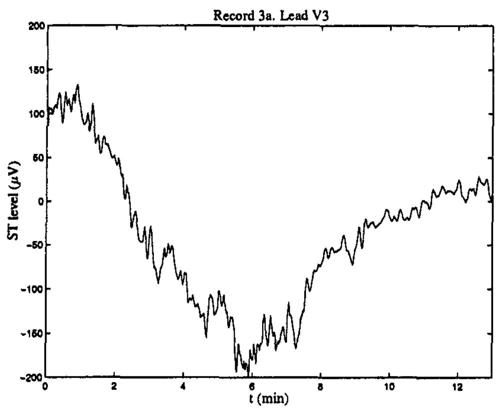


Figure 1. ST level trend example during stress test.

From the ST level trends, a value (for each lead) of ST deviation (ΔST) was estimated at the maximal stress point with respect to the basal measurement. A total of 10 and 15 beats were selected from the stress peak and first instants of recording at rest, respectively, to calculate the median ST values representative of both stages. The ST deviation corrected by the HR (ΔST/ΔHR) was also considered in the study.

QRS waves amplitude changes

The onset, peak and offset of the different ECG waveforms were detected by using the automated detector of waveform boundaries described in [3]. The detector has been previously validated attending to the time location of the ECG points using cardiologists' measurements [4]. For the purposes of the present work, the detector was validated also for the measurement of wave amplitudes. A set of 490 beats were extracted and printed from the first seconds of 49 stress test recordings, and two cardiologists were asked to manually measure the R wave and RS peak-to-peak amplitudes in one lead. The comparative statistics (mean, μ; standard deviation, σ; and correlation coefficient, r) between the cardiologists' measurements and with respect to those given by the automatic detector are shown in Tab. 1 and Tab. 2, respectively. Differences between each cardiologist's measurements and automatic ones were of the same order than differences between the two cardiologists. This validation provides high confidence when automatic waveform amplitude delineation is performed.

Table 1. R wave amplitude validation (all measurements expressed in μV).

R wave	Card. 2 ($\mu \pm \sigma, r$)	Autom. ($\mu \pm \sigma, r$)
Card. 1	$25 \pm 50, 0.99$	$-13 \pm 60, 0.99$
Card. 2	—	$-39 \pm 62, 0.99$

Table 2. RS amplitude validation (all measurements expressed in μV).

RS	Card. 2 ($\mu \pm \sigma, r$)	Autom. ($\mu \pm \sigma, r$)
Card. 1	$14 \pm 57, 1.00$	$-23 \pm 74, 0.99$
Card. 2	—	$-36 \pm 83, 0.99$

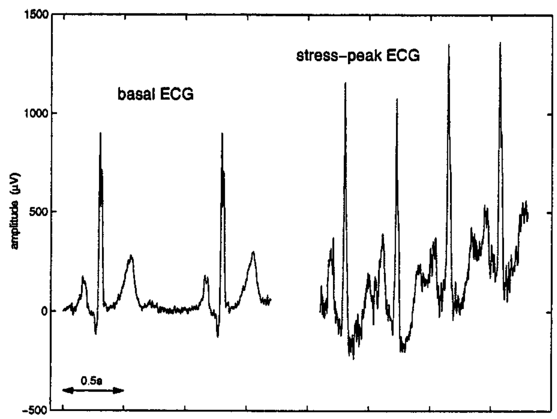
The detector was applied to the exercise ECG recordings and Q, R and S waves amplitudes, and QRS duration were estimated. The corresponding deviations of these indexes (Δ defined as difference between stress peak and rest values) were derived from the trends in a similar way than that described for ΔST.

2.3. Statistical analysis

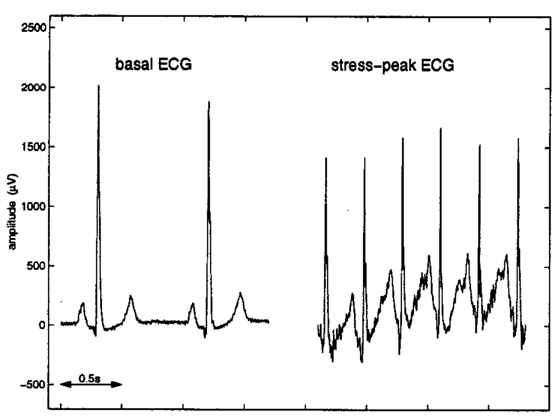
Multivariate discriminant analysis [5] was used to classify the patients in the different groups. The variations of the different clinical indexes estimated during the stress test period (Δ) were considered as variables in the analysis. The *prior probabilities* for the groups were considered independent from the groups sizes to avoid inclusion of a priori information. We used in the analysis the *stepwise* method that permits the reduction in the number of variables included in the discrimination, identifying those that are good predictors for the classification. The criterion followed in the variables inclusion/rejection was the *Wilks' lambda* minimization. The classification results were calculated with the cross-validated estimation (or *leave-one-out*), in which each case is classified by the functions derived from the remaining cases. The cross-validated method is more realistic in the sense that each case to be classified is not used in the model derivation.

3. Results

Differences in the ECG signal during basal and stress peak conditions were usually significant, but the interest lies in whether these differences showed a different pattern in the two groups of patients (see Fig.2).



(a) Ischemic patient.



(b) Healthy subject.

Figure 2. ECG morphologies during basal and stress peak.

Multivariate discriminant analysis was independently applied to different sets of indexes deriving a discriminant function (composed of six variables -same number as in Athens QRS score definition [1]- automatically selected from each set) to get the best classification. First, we used the Athens QRS score as previously defined, then we included ΔQ, ΔR and ΔS amplitudes measured on all leads and leaving the method to find the best linear combination or discriminant function. Afterwards we considered ST deviations as variables in the analysis, ST deviations corrected by the heart rate ($\Delta ST/\Delta HR$), QRS duration intervals (ΔQRS_d) and finally all these variables together in a unique set.

The results of classification using the different sets of variables are shown in the *confusion matrices* represented in Tab. 3. A summary of the results in terms of sensitivity (Se), specificity (Sp), positive and negative predictive values (+P and -P, respectively) and exactness (Ex) is shown in Tab. 4. The coefficients of the selected variables obtained in the discriminant functions are represented in Tab. 5.

Table 3. Confusion matrices obtained with different clinical indexes.

		Prediction		
	Group	healthy	ischemic	Total
Athens Score	healthy	41	14	55
	ischemic	13	16	29
$\Delta Q\ \Delta R\ \Delta S$	healthy	39	16	55
	ischemic	6	23	29
ΔST	healthy	38	17	55
	ischemic	13	16	29
$\Delta ST/\Delta HR$	healthy	41	14	55
	ischemic	14	15	29
* ΔQRS_d	healthy	30	21	51
	ischemic	10	19	29
combined	healthy	45	10	55
	ischemic	7	22	29

*For ΔQRS_d variables the healthy group was reduced to 51 patients due to the impossibility to measure all the variables in 4 patients.

Table 4. Summary results of classification.

Variables	Se	Sp	+P	-P	Ex
Athens Score	55.2	74.5	53.3	75.9	67.9
$\Delta Q\ \Delta R\ \Delta S$	79.3	70.9	59.0	86.7	73.8
ΔST	55.2	69.1	48.5	74.5	64.3
$\Delta ST/\Delta HR$	51.7	74.5	51.7	74.5	66.7
ΔQRS_d	65.5	58.8	47.5	75.0	61.3
combined	75.9	81.8	68.7	86.5	79.8

The use of the Athens QRS score slightly improved the specificity with respect to the use of ST deviations (see Tab. 4). However when the Q, R and S waves amplitudes in all leads were considered, the analysis increased the sensitivity from 55% to 79%, with no large change in specificity. The use of HR-corrected ST deviations did not significantly affect the results, and QRS duration variables showed lower classification rates. Best results were obtained when a six variables set selected from all the indexes was used, with Se/Sp values of 76/82%, respectively. ΔQ measured in lead aVF was the most significant variable in all the sets where it was included (see coefficients in Tab. 5) .

Table 5. Coefficients of the discriminant functions.

Athens Score	ΔQ_{aVF}	ΔQ_{V5}	ΔR_{aVF}	ΔR_{V5}	ΔS_{aVF}	ΔS_{V5}
	1	1	- 1	- 1	1	1
$\Delta Q, R, S$	ΔQ_{aVF}	ΔR_{I}	ΔQ_{aVL}	ΔS_{I}	ΔR_{aVL}	ΔS_{V4}
	.866	.908	.415	-.576	-.498	.334
ΔST	aVF	V6	RV4	V3	V4	II
	.631	-.454	.781	-.792	.406	.484
$\Delta ST/\Delta HR$	V5	aVL	V4	RV4	II	V6
	-.841	-.182	.441	.627	1.018	-.313
ΔQRS_d	RV4	I	V5	V6	aVF	II
	.970	-.638	.103	-.040	-.524	.477
combined	ΔQ_{aVF}	$\Delta QRS_{d\,RV4}$	$\Delta QRS_{d\,aVR}$	ΔQ_{aVL}	$\Delta QRS_{d\,V4}$	$\Delta ST/\Delta HR_{aVR}$
	.851	-.169	.512	.458	-.415	.360

4. Discussion

The high noise content in the ECG during stress (mainly present as muscular noise and baseline wandering) is one of the major problems to correctly estimate the clinical indexes, especially when the waveforms are of small amplitude. This effect has been considered and reduced as much as possible.

Other effect which highly influences the measure of waves amplitudes is the respiration modulation. In a more advanced approach this should be compensated to provide better reliability in the estimation of amplitude values.

The RV4 lead was acquired to extract more information from the right part of the chest and although it was not significant for Q, R and S waves amplitudes indexes, it was included in the discriminant function when measuring ST deviations.

The clinical indexes which showed the best identification of the two groups corresponded to Q, R and S amplitude variables measured on different leads (not only in aVF and V5 as the Athens QRS score proposes). However this selection of variables and coefficients might be somehow influenced by the group of patients and a different set of parameters could be the best in a different population.

The use of Q, R and S amplitude variables with respect to ST deviations increased the sensitivity of the test but did not significantly affect the specificity. This result is in agreement with those results found in [1].

5. Conclusions

Results showed that a combination of QRS amplitude changes may provide a closer description of the heart response to exercise than ST deviations do, increasing the sensitivity in around 25% while maintaining the same level of specificity. The combined use of indexes from repolarization and depolarization periods could be even more suitable to classify patients. Further research using a larger population is needed to achieve generality for these results.

Acknowledgements

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