Coherence Between Heart Rate and Dominant Frequency of the Time-frequency Heart Rate Variability Spectrum as Ischemic Marker in the Exercise Test

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Abstract

Observation on Heart Rate (HR) and Heart Rate Variability (HRV) trends in exercise ECGs lead us to hypothesize that some correlation exists between the evolution of HR and the dominant HRV frequency, which may differ in ischemic and healthy subjects. The ECGs recordings from stress test trials were collected and clustered into four groups: ischemic (positive coronary angiography), non-ischemic, volunteers and healthy (non-ischemic patients with 10 year predicted risk of CAD < 5% , according to the Framingham index). A new index based on the coherence between HR and dominant frequency of the time-frequency HRV was proposed in this work to add diagnostic information to exercise testing, obtaining statistically significant differences ($p<10^{-5}$) between ischemic and rest of the groups.

1. Introduction

The traditional interpretation of exercise ECG for diagnosis of coronary artery disease (CAD) is based on the ST segment depression during an exercise trial [1].

The low specificity of ST segment based tests poses the search for alternative methods, such as medical images. However, these methods are usually more expensive and sometimes invasive.

Some works have related heart rate variability (HRV) measurements during ambulatory monitoring to ischemia [2]. In this work, we propose a new approach for extracting information from HRV to improve the diagnostic value of exercise test. HRV during exercise is non-stationary, reaching frequencies well over the standard 0.4 Hz. Therefore, HRV is dynamically analysed in order to obtain its central (mean) frequency as a function of time, aimed to be a gross measurement of the central nervous system (CNS) action. A new parameter, the coherence factor, is computed for each patient from the coherence between the time-dependant mean central frequency series and the heart rate (HR) itself. The coherence factor has been statistically compared among different diagnostic groups: *ischemic*, *non-isch*emic, *volunteers* and *healthy*.

The goal of this work is to evaluate the diagnostic ability of the described parameter (the coherence factor) and its use to differentiate groups of patients and improve stress test sensitivity/specificity.

2. Methods

2.1. Study population

In the University Hospital of Zaragoza, ECGs of 811 patients undergoing treadmill (Bruce protocol) exercise test were recorded, including 66 non-ischemic volunteers. Standard leads (V1, V3-V6, I, II, III, aVR, aVL y aVF) and RV4 (substituting classical V2 to extract more information from the right part of the heart) were digitally recorded (1 kHz sampling rate, amplitude resolution of 0.6 µV).

Patients were classified into four groups: *ischemic*, *non-ischemic*, *healthy* and *volunteers*. The *ischemic* group was composed of 73 patients with significant stenoses in at least one major coronary artery from coronary angiography. The *non-ischemic* group included 220 patients with negative clinical and electrical exercise test and reaching at least 90% of the maximal (age-related) heart rate and 66 volunteers from Spanish Army (with negative exercise test). The *healthy* group was composed of 69 *non-ischemic* patients with risk of coronary event in the following 10 years lower than 5% according to Framingham index [6]–[7]. The remaining 452 non-classified patients were not analysed in this study.

2.2. Measurements

ECG signal preprocessing is performed before HRV measurement: detection and selection of beats, removing ectopic ones, cubic splines baseline wander attenuation and rejection of beats whose difference in the isoelectric level with respect to adjacent beats is more than 600 µV. Then, HR trends are computed and filtered in order to remove registers with visually detectable artefacts which would mask the frequencies of interest. Finally, HRV is analysed for a set of 243 patients (41 *ischemic*, 45 *volunteers*, 157 *non-ischemic* and 53 *healthy*).

For each patient the HR trend (Figure 1) is linearly interpolated to be uniformly sampled, segmented and linearly detrended resulting in the HR signal *hr(t)*. The spectrogram $S_{hr}(t,f)$ (time-frequency analysis) is obtained according to expression (1), where *h(t)* is the Hamming window. Thus, the frequency analysis gives information of fast fluctuations in the HR, without taking into account the baseline variation (very emphatic during an exercise test).

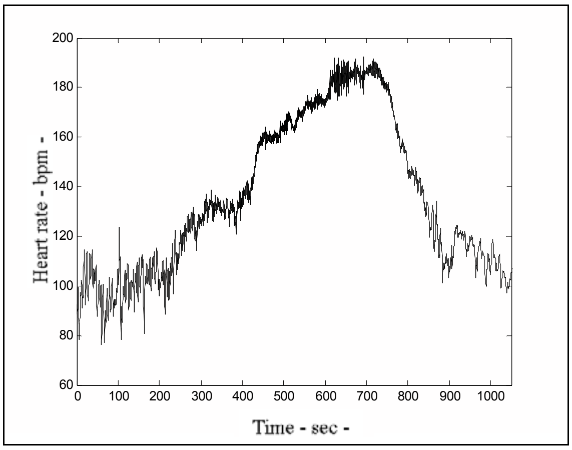


Figure 1. Heart Rate trend in an exercise (volunteer patient)

$$S_{hr}(t,f) = \left| \int_{-\infty}^{\infty} hr(u) \cdot h^{*}(u-t) \cdot e^{-j2\pi f u} \cdot du \right|^{2} \qquad (1)$$

The result is an image representing the power level for each frequency during the realization of the exercise (Figure 2).

The next step is to calculate the central frequency $f_c(t)$ (Figure 3) of each spectrogram, according to expression (2). Thereby, it is obtained a dynamic measurement of the dominant frequency during the exercise test, getting a gross estimation of frequency at which the central nervous system frequency acts.

$$f_c(t) = \frac{\int_{-\infty}^{\infty} f_i(t) \cdot |S_{hrx}(t, f_i)|}{\int_{-\infty}^{\infty} |S_{hr}(t, f_i)|} \qquad (2)$$

In order to get a new parameter to differentiate patients, it is obtained the coherence factor between the HR series and the central frequency $f_c(t)$ series – expression (3) –, after observing the similarity (coherence) between them in healthy patients, and resulting less evident in ischemic patients.

$$C_{HR \cdot f_c} = \frac{\langle HR, f_c \rangle}{\sqrt{\|HR\| \cdot \|f_c\|}} \qquad (3)$$

where < , > denotes the scalar product.

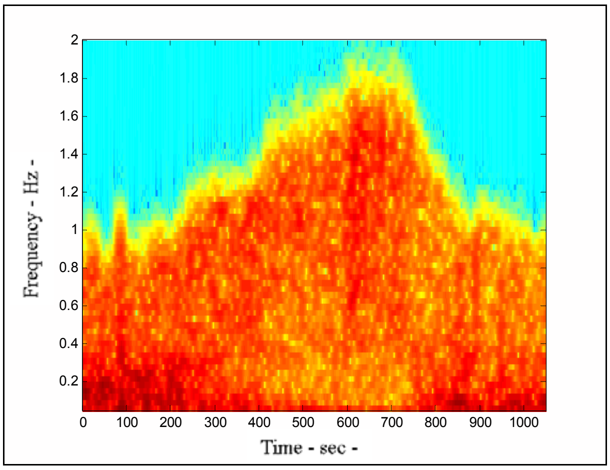


Figure 2. Spectrogram (time-frequency) for the HR trend in Figure 1.

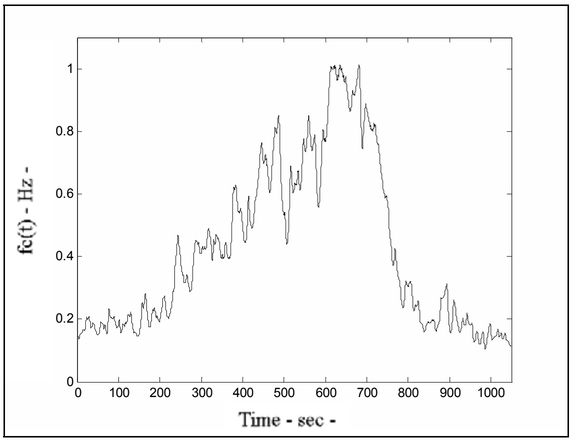


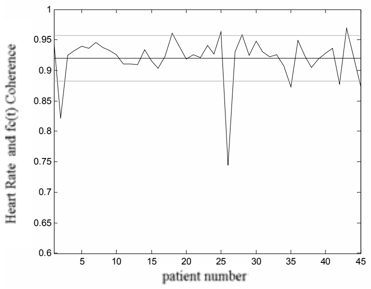
Figure 3. Central Frequency $f_c(t)$ evaluated for the subject in Figure 1.

After evaluating the coherence factor for each subject, a statistical analysis is carried out, getting the mean and standard deviation (SD) values for each group: *ischemic*, *non-ischemic*, *volunteers* and *healthy*. A significance test has been performed (*t-Student*) to evaluate the ability of this new index to differentiate between the study groups.

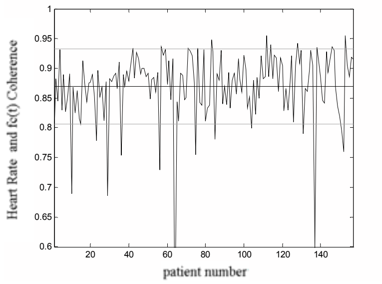
3. Results

Figure 4 shows the coherence factor for each patient group. It can be observed in the *ischemic* group lower mean and higher SD values than in the other groups, indicating a great variability. Results of mean and SD values are summarized in Table 1.

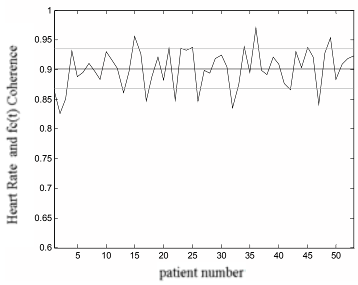
Separation between *volunteers* and *healthy* is the smallest, but also significant. This indicates that the Framingham index is very restrictive to assure the absence of coronary problem risk. However, since the result is comparable to volunteers, it confirms the reliability of the classification.



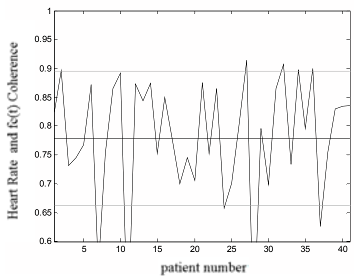
(a) Volunteers “V”



(b) Non-ischemic “NI”



(c) Healthy “H”



(d) Ischemic “I”

Figure 4. Coherence between HR series and central frequency series for each group of subjects.

Table 1. Mean (μ) and SD (σ). Coherence factor.

	I	V	H	NI
μ	0.7786	0.9202	0.9017	0.8695
σ	0.1163	0.0372	0.0331	0.0682

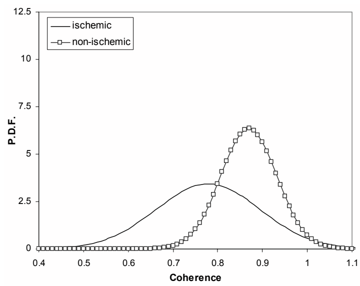
Table 2 shows results for the *t-Student* test. Comparing the *ischemic* group with the non-ischemic patients (*non-ischemic* with negative exercise test, physically prepared *volunteers* and *healthy*, according to Framingham index) it can be observed that the greatest differentiation exists between *ischemic* and *volunteers* groups, as it was expected since the last ones are supposed to enjoy better health than the *ischemic,* and even than the *non-ischemic*. However, it is also observed a clear separation between the *ischemic* and *non-ischemic* groups.

Table 2. Statistical results. *t-Student* test. Comparison of groups in pairs.

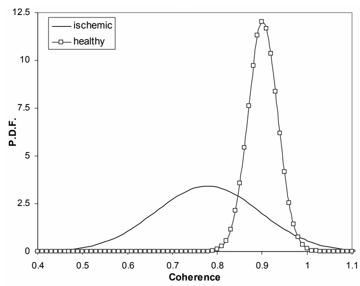
	p		*p*
I-V	3.33E-13	V-H	1.43E-02
I-NI	3.46E-06	V-NI	4.121E-11
I-H	1.62E-10	H-NI	4.967E-06

Figure 5 shows the probability distribution functions, assumed Gaussian, for each group of subjects, compared in pairs, once checked the fitting to this distribution. It can be appreciated visually the separation between pairs (higher between *ischemic* and *volunteers*) and the different deviations (higher variability for the *ischemic* group, making more difficult its differentiation).

The Framingham index allows to stratify patients without ischemic risk in a restrictive way, as it can be seen in Figure 5. The *healthy* (stated by Framingham index) and the *volunteers* groups are very similar, although the last one consists of younger and presumably healthier population than the first one.



(a)



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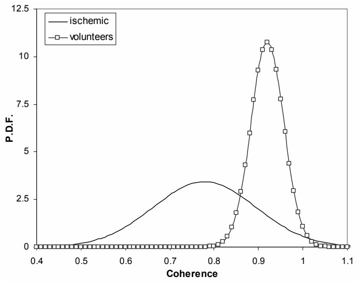

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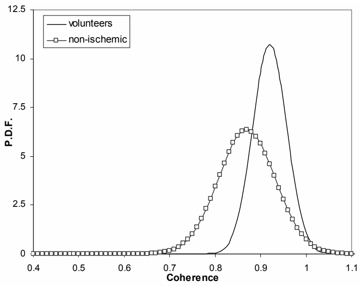
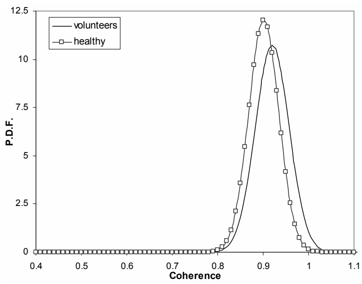


(d)



(e)

Figure 5. Normal distribution of coherence, according to the mean and SD measured. Comparison of groups in pairs.

4. Conclusions and discussion

Correlation between HR and its variability, according to this study, could add new diagnostic information to the classical ST and QRS measurements in exercise testing. Our data show the ability of this new parameter, the coherence factor, to differentiate subjects.

This correlation is significantly lower in *ischemic* than in *non-ischemic* patients. High values of correlation correspond to the diagnostic value given by the Framingham index for healthy subjects.

In order to validate the new index, the whole development of the exercise test should be guaranteed to have a marked excursion of the HR. The eventual lack of coherence could be due to a small HR excursion, invalidating the results.

Further research is needed to confirm our findings in larger prospective populations and to study the complementarity with ST values.

Acknowledgements

This work has been supported by the projects TIC2001-2167-CO2-02 from CICYT/FEDER and P075-2001 from CONSI+D/DGA, Spain.

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