Very-Low-Frequency Modulation of QRS slopes in Patients with Angina Pectoris

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Abstract

This study was designed to investigate very-low-frequency modulation of QRS slopes in control electrocardiographic recordings of patients with stable angina pectoris admitted for prolonged elective percutaneous coronary intervention (PCI). This modulation occurs between 0.01Hz and 0.07Hz and has been described for QRS slopes as well as for heart rate variability (HRV). Results shows that power spectrum area in the modulation band (MB) and in the high-frequency (HF) band are larger for QRS downslope (I_{DS}) than QRS upslope (I_{US}). A differential Autonomic Nervous System (ANS) regulation at different ventricular regions, in addition to respiration or other mechanical effects, could explain this behavior. The same modulation was found in HRV and our results suggest that a relation between QRS slopes and HRV modulation exists. Whatever the source of the MB modulation is, its effect is much lower, in relative terms, for QRS slopes than for HRV.

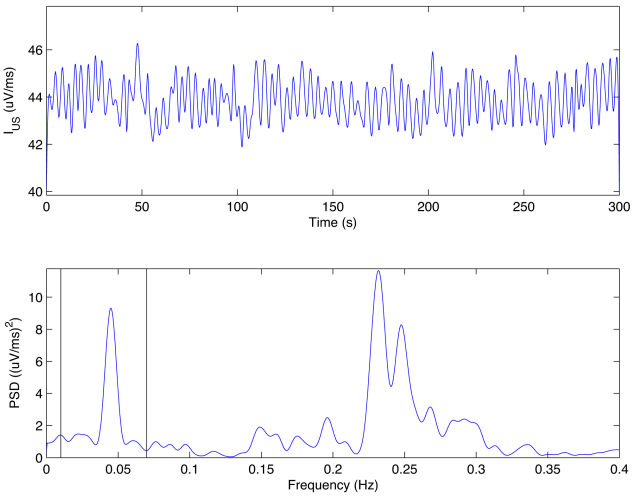

Figure 1. Downward slope (I_{DS}) for lead V6 (top) and its spectra (bottom) where vertical lines delimit modulation band.

1. Introduction

Angina pectoris is a severe chest pain produced by ischemia of heart muscle induced by the reduction of blood supply to the myocardium due to blockage of one or more coronary arteries.

Heart rate variability (HRV) is widely used as a non-invasive method for assessing autonomic nervous system (ANS) activity on the heart and the balance between sympathetic and parasympathetic systems; it is divided in three well known bands: 1) Very-Low-Frequency (VLF) band (0.003 - 0.04Hz); 2) Low-Frequency (LF) band (0.04 - 0.15Hz); 3) High-Frequency (HF) band (0.15 - 0.4Hz) [1]. In the setting of myocardial ischemia and infarction, HRV is also used as a mortality prediction index [2, 3]. Mechanisms underlying the VLF components of HRV are controversial and have been associated to thermoregulation [4], renin-angiotensin-aldosterone systems and/or parasympathetic outflow [5].

QRS slopes have been used for quantifying ischemia-induced depolarization changes on the electrocardiogram (ECG) and have been shown to be a robust surrogate of amplitude variations on the QRS complex [6]. In patients with stable angina pectoris a very-low-frequency modulation of QRS amplitude measured through upward (I_{US}) and downward (I_{DS}) QRS slopes (see Figure 1) of uncertain origin has been reported [7]. The frequency range of this modulation has been shown to lie between 0.01 and 0.07Hz, here denoted as modulation band (MB), which is a modification of the usually studied VLF band [7]. This modulation has been related to very-low or low-frequency components in HRV and has been postulated as an attenuated effect of the modulation observed in periodic breathing [8].

The objective of this work is to study this very-low-frequency modulation of QRS slopes and its relationship

with ANS interaction reflected through HRV regulation.

2. Materials

The database used in this work contains ECG recordings of patients with stable angina pectoris admitted for prolonged elective PCI in the Charleston Area Medical Center in West Virginia, USA (STAFF III dataset). The study population is composed of 60 patients in which 5-minutes length ECG control recordings were acquired before coronary intervention. ECG signals contain nine standard leads (V1−V6, I, II and III) and were digitized at 1 kHz sampling rate with an amplitude resolution of 0.6 μV.

3. Methods

3.1. QRS slopes from spatial QRS loop-projected lead

ECG signals were pre-processed before the analysis, including 1) QRS complex detection and normal beats selection according to [9]; 2) baseline drift attenuation via cubic spline interpolation.

The vectocardiogram (VCG) was computed using the inverse Dower matrix on leads V1−V6, I and II [10], obtaining three orthogonal leads $x(n), y(n)$ and $z(n)$ that allow to represent the evolution of the cardiac electrical vector in 3D space. During depolarization, the dominant direction $\mathbf{u}$ of the QRS loop points to the QRS loop tip, called *mean electrical axis*.

The dominant direction of each QRS complex was determined as:

$$\mathbf{u} = [x(k_0), y(k_0), z(k_0)]^T, \tag{1}$$

with

$$k_0 = arg\max_k \{x(k)^2 + y(k)^2 + z(k)^2\} \tag{2}$$

where k spans from 20 ms before to 130 ms after QRS complex onset [7]. A new projected lead $d(n)$ was calculated by projecting the points of the QRS loop onto this $\mathbf{u}$ axis:

$$d(n) = \frac{[x(n), y(n), z(n)]\mathbf{u}}{||\mathbf{u}||} \tag{3}$$

The projected lead $d(n)$ was delineated using a wavelet-based algorithm [11] and the following indices were computed following the methodology described in [7]:

1) I_{US} : Upward slope of the R wave.
2) I_{DS} : Downward slope of the R wave.

3.2. Heart rate variability

Before HRV computation, ectopic beats and misdetections were pre-processed using an algorithm based on Integral Pulse Frequency Modulation model (IPFM) in order to obtain better assessment of the HRV information [12]. The HRV signal was computed from the corrected event series based on the IPFM model [13].

3.3. Spectral analysis

The Power Spectral Density (PSD) was estimated using Welch's periodogram over half-overlapped 1.6-minute segments for the 4 Hz cubic spline interpolated series of slopes (I_{US} and I_{DS}) and HRV signal. For each spectra the following indices were obtained:

1) P_{MB} : Power area in MB band (0.01 to 0.07 Hz).
2) P_{HF} : Power area in HF band (0.15 to 0.4Hz).
3) $R_{\text{HF/MB}}$: Ratio between P_{HF} and P_{MB}.

Mean and standard deviation (SD) of those above indices were computed. The Wilcoxon test for paired samples was used for statistical comparisons.

4. Results

4.1. Spectral indices study

Table 1 shows that there is significantly more power in I_{DS} than in I_{US} ($p < 0.05$) for both MB and HF bands; in addition, there is no statistically significant difference ($p > 0.05$) in $R_{\text{HF/MB}}$ between I_{DS} and I_{US}.

Table 1. Mean ± SD of power spectrum area of P_{MB}, P_{HF} and $R_{\text{HF/MB}}$ indices for QRS slopes.

Slope	P_{MB} $(\mu V/ms)^2$	P_{HF} $(\mu V/ms)^2$	$R_{\text{HF/MB}}$
I_{US}	3834 ± 5441	6288 ± 5857	3.79 ± 3.78
I_{DS}	4955 ± 6643	9260 ± 8482	4.13 ± 4.53

Respiration or other mechanical sources would be expected to similarly influence I_{DS} and I_{US}. The results presented in Table 1 do not reject those contributions, which might be the most relevant source underlying MB modulation of QRS slopes but do not discard additional mechanisms related to differential Autonomic Nervous System (ANS) regulation at distinct ventricular regions.

In the case of HRV, Table 2 shows that there is significantly more power area ($p < 0.05$) in MB band than in HF band, which is in relative concordance with results reported by other authors for patients with heart failure [2,3].

Table 2. Mean ± SD of power spectrum area of P_{MB}, P_{HF} and $R_{HF/MB}$ indices for HRV.

P_{MB} (ms^2)	P_{HF} (ms^2)	$R_{HF/MB}$
3.28 ± 5.39	0.9 ± 1.79	0.4 ± 0.45

4.2. Relationship between QRS slopes and HRV modulation

A similar modulation was found in QRS slopes and HRV signal, as illustrated in Figure 2 and corroborated by visual inspection of the spectral peaks for all of the recordings analyzed in this study. Additionally, spectral coherence was computed, and maximal values in MB band of 0.879 ± 0.085 and 0.853 ± 0.111 were for coherence of HRV with I_{US} and I_{DS}, respectively.

Further analysis included the comparison between $R_{HF/MB}$ for QRS slopes and HRV which was performed by expressing:

$$R_{HF/MB}|_{I_{XS}} = \alpha \cdot R_{HF/MB}|_{HRV} \quad (4)$$

where subindex X denotes either upward ($X \equiv U$) or downward ($X \equiv D$) QRS slope. Table 3 shows that α factor in (4) is very high, so whatever the origin of the modulation in MB band is, it is much lower, in relative terms, for QRS slopes than for HRV. This situation is probably given by the fact that HRV at MB is affected by other factors in addition to those affecting the QRS slopes modulation.

Table 3. Mean ± SD of α factor between QRS slopes and HRV.

Slope	α
I_{US}	27.76 ± 54.02
I_{DS}	31.56 ± 56.91

5. Discussion and conclusion

This work focuses on investigating a very-low-frequency modulation of QRS slopes in electrocardiographic control recordings of patients with angina pectoris. Additionally its relationship with the same modulation in the HRV.

The origin of the observed oscillations is unclear. Differential amount of power area in the spectra of I_{US} and I_{DS} do not discard the possibility that sources additional to respiration might be involved, which could include a differential ANS regulation at different ventricular regions. The same modulation found in the QRS slopes was found in HRV, and then connection between these two effects may

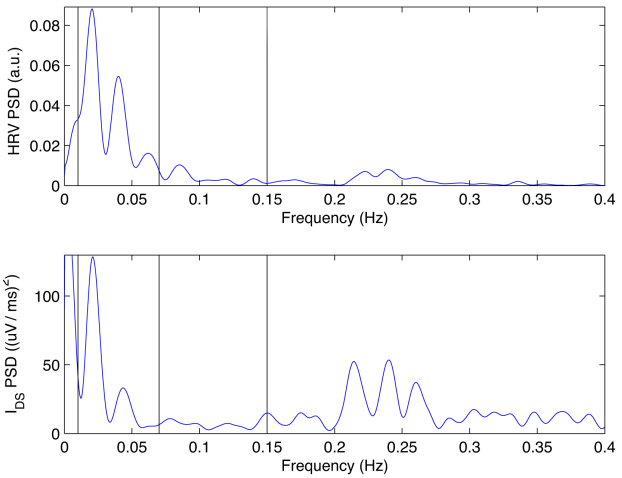

Figure 2. PSD of HRV signal (top) and I_{DS} (bottom) where can see similar components at frequencies nearly 0.2Hz and 0.4Hz; in vertical lines, MB and HF bands are delimited.

exist. Whatever the source of the effect is, it is significantly lower, in relative terms, for slopes than for HRV (factor 27 and 31 in the comparison between HRV and I_{US} and I_{DS} respectively). Other factors different from those modulating QRS slopes may be involved in the modulation of HRV.

In addition, in the case of HRV there is significantly more power area in MB band than in HF band, which is consistent with results reported by other authors for patients with heart failures [2, 3].

The lead where QRS slopes were measured and MB modulation was studied was a loop-projected lead. This is to maximize the information related to the QRS, since the QRS loop-projected lead is obtained by projecting the VCG onto the direction of maximal projection, thus obtaining a single lead that maximizes the signal to noise ratio.

The results presented here open the door for future works that should evaluate the modulation of ECG amplitude in MB band by ANS-related effects and respiration, and explore their potential clinical implication in cases of apnea other respiration-related disorders [14].

Acknowledgements

This work was supported by a personal grant to Alejandro Alcaine from Education Ministry of Spanish Government through collaboration program in research initiation oriented to undergraduate students, by MCyT and FEDER Spain under Projects TEC2010-21703-C03-02 and TEC2010-19410 and by Grupo Consolidado GTC and project PI 144/2009 from Gobierno de Aragón, Spain. The CIBER is an initiative of Instituto de Salud Carlos III.

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