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To cite this version:

Miguel Altuve, Sara Wong, Gianfranco Passariello, Guy Carrault, Alfredo Hernández. LF/(LF+HF) index in ventricular repolarization variability correlated and uncorrelated with heart rate variability.. Conference proceedings : .. Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference, Institute of Electrical and Electronics Engineers (IEEE), 2006, 1, pp.1363-6. 10.1109/IEMBS.2006.259821 . inserm-00656264

HAL Id: inserm-00656264
https://www.hal.inserm.fr/inserm-00656264
Submitted on 3 Jan 2012

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LF/(LF+HF) index in Ventricular Repolarization Variability correlated and uncorrelated with Heart Rate Variability

M. Altuve, Student Member, IEEE, S. Wong, G. Passariello, G. Carrault, A. Hernández.

Abstract—The purpose of this study, was to assess whether LF/(LF+HF) obtained from ventricular repolarization variability (VRV) reflects the state of sympathovagal balance. The VRV time series and Heart Rate Variability (HRV) time series from seventy two electrocardiogram (ECG) records in four different Autonomic Nervous System (ANS) profiles (athletes, cardiac transplant patient, heart failure patients and normal subjects) were extracted. A dynamic linear parametric model was applied to separate the VRV in two parts, VRV correlated with HRV (VRVc) and VRV uncorrelated with HRV (VRVu). Spectral indices were obtained from HRV, VRV, VRVc and VRVu time series. Changes of these indicators from rest to tilt position were analyzed. Results showed that: i) only LF/(LF+HF) from HRV time series increases significantly from rest to tilt in all ANS profiles, this information could not be retrieved in the other three series (VRV, VRVc and VRVu), ii) LF/(LF+HF) index in HRV series are significantly different between normal subjects and heart failure patients, while cardiac transplant patients show a low coherence between HRV and VRV power spectra and iii) HF rhythm in VRV series seem to related to the mechanical effect of respiration.

I. INTRODUCTION

A great number of works have sought to establish relations between the variability of the ventricular repolarization (VRV) and heart rate variability (HRV). Peaks in the low frequency (LF) and high frequency (HF) bands were observed in the power spectra of the VRV and the HRV time series [1]. Additionally, it was found that the power distribution between LF and HF in the VRV power spectrum was reversed with respect to heart rate power spectrum. Generally, LF/(LF+HF)HRV is higher than 0.5 and LF/(LF+HF)VRV is smaller than this value. However, the physiological origins of these components are explained partially and the interpretation of the spectral parameters resulting from VRV sequence remains incomplete [2].

Moreover, a recent work using multiple correspondence analysis shows that low frequencies of the HRV and VRV series were correlated [3]. In that work, high frequencies of the VRV space seem to be inadequate markers for the characterization of the Autonomic Nervous System (ANS). However, they observed that using only VRV parameters additional information from the population was obtained. These controversial results led us to explore a dynamic linear parametric model to quantify the dependence of ventricular repolarization variability to heart rate variability. This model allows separation of VRV series into a series correlated and uncorrelated with HRV [4]. The uncorrelation between VRV and HRV does not imply that there is not any physiological dependence between them [5].

In order to better understand the relationships between heart rate and ventricular repolarization phenomena, this model appears as an interesting tool to explore the value of the index LF/(LF+HF) in VRV correlated and VRV uncorrelated to HRV series.

The aims of this study were: i) to study LF/(LF+HF) of VRV from correlated and uncorrelated series, to reflect the state of sympathovagal balance in resting position, ii) to compare LF/(LF+HF) index in four different ANS profiles: athlete subjects, cardiac transplant patients, heart failure patients, and normal subjects.

II. METHODS

A. Model Formulation

The model was based on the one proposed by Porta et al. [4]. It analyzes the beat-to-beat series of the HRV series from the RR durations and VRV series from the RT apex (RT max) periods. From these two signals, a parametric identification procedure and spectral decomposition techniques allow to separate VRV series into VRV correlated to HRV series (VRVc) and VRV uncorrelated to HRV series (VRVu). The transfer function VRV-HRV can thus be determined (Figure 1).

\[ A_{11}, A_{12}, A_{22} \text{ and } D_1 \] are polynomials of order \( n \) in the \( z^{-1} \) domain. \( W_{HRV} \) and \( W_{VRV} \) are zero-mean white noises with variance \( \lambda^2_{HRV} \) and \( \lambda^2_{VRV} \), respectively. The polynomial \( A_{22} \) can be estimated using a least squares approach, and the \( A_{11}, A_{12} \text{ and } D_1 \) can be obtained using a generalized least squares (GLS) methodology [4, 5].

The model order \( n \) is chosen inside the set \{8,10,12\}, according to the minimum of the Akaike figure of merit [6]. As no a priori information was used, all blocks of the model are of the same order, thus, not giving an advantage to one
From figure 1, two transfer functions can be identified. The first one, \( H_1(z) = 1/(D_1(z)A_{h1}(z)) \), has as output the VRV uncorrelated to HRV (\( \text{VRV}_u \)), which is supposed to be the ANS action to the VRV. The second one, \( H_2(z) = A_{h2}(z)/(A_{h2}(z)A_{h1}(z)) \), has as output the VRV correlated to HRV (\( \text{VRV}_r \)) and it is supposed to reflect the modulation of the HRV with respect to VRV.

RR series was modeled as a \( n \) order autoregressive (AR) stationary process given by equation 1, and VRV series, given by equations 2 and 3, was the result of two uncorrelated processes (ARARX model, [7])

\[
\text{HRV}[i] = -\sum_{k=1}^{n} a_{2k}[k] \text{HRV}[i-k] + W_{\text{HRV}}[i] \tag{1}
\]

\[
\text{VRV}[i] = \sum_{k=0}^{n} a_{1k}[k] \text{HRV}[i-k] - \sum_{k=1}^{n} a_{1k}[k] \text{VRV}[i-k] + N_{\text{VRV}}[i] \tag{2}
\]

\[
N_{\text{VRV}}[i] = -\sum_{k=1}^{n} d_{1k}[k] N_{\text{VRV}}[i-k] + W_{\text{VRV}}[i] \tag{3}
\]

Because of the uncorrelation between inputs \( W_{\text{HRV}} \) and \( W_{\text{VRV}} \), the power spectral density of VRV (\( S_{\text{VRV}} \)) can be computed as the sum of the two partial power spectra that express the contribution of each source:

\[
S_{\text{VRV}}(f) = S_{\text{VRV}_u}(f) + S_{\text{VRV}_r}(f)
\]

The model was applied using criteria of a mean coherence of 0.5. The model order was fixed using sine waves of frequencies corresponding to LF and HF components. Akaike criterion was used to select the model order [6].

The HRV and VRV sequences were obtained using the Gritzali QRS detector followed by a manual verification of each detected R-wave [8]. VRV sequences were obtained by applying the algorithm proposed by Vila et al. [9]. Artifacts in the VRV sequence were also manually removed.

\[
\text{Modulation of the HRV with respect to VRV.}
\]

\[
\text{Uncorrelated sources (ARARX model, [7])}
\]

\[
\text{Given by equations 2 and 3, was the result of two stationary processes given by equation 1, and VRV series, expressed the contribution of each source:}
\]

\[
N_{\text{VRV}}[i] = -\sum_{k=1}^{n} d_{1k}[k] N_{\text{VRV}}[i-k] + W_{\text{VRV}}[i]
\]

\[
S_{\text{VRV}}(f) = S_{\text{VRV}_u}(f) + S_{\text{VRV}_r}(f)
\]

\[
\text{Because of the uncorrelation between inputs} \ W_{\text{HRV}} \text{and} \ W_{\text{VRV}}, \text{the power spectral density of VRV} \ (S_{\text{VRV}}) \text{can be computed as the sum of the two partial power spectra that express the contribution of each source:}
\]

\[
\text{HRV and VRV Series}
\]

HRV sequences were obtained using the Gritzali QRS detector followed by a manual verification of each detected R-wave [8]. VRV sequences were obtained by applying the algorithm proposed by Vila et al. [9]. Artifacts in the VRV sequence were also manually removed.

\[
\text{D. Spectral Analysis}
\]

The HRV and VRV sequences were linearly interpolated and uniformly sampled at 2 Hz. A time-varying autoregressive modeling of the interpolated HRV and VRV sequences was performed by using a 25 seconds sliding window. Power spectral densities were estimated. For each test the following parameters were determined: \( L_{\text{HRV}}/L_{\text{VRV}}, L_{\text{HF}}/L_{\text{HF}} \) for HRV sequences, and \( L_{\text{VRV}}/L_{\text{HF}} \) for VRV sequences. The LF and HF bands were defined respectively by [0.04-0.15 Hz] and by [0.15-0.4 Hz] as proposed in [10].

\[
\text{E. Parametric Model}
\]

In order to illustrate, in a simple way, the operation of the model, it was validated using sine waves of frequencies corresponding to LF and HF components. Akaike criterion was used to select the model order [6].

Tables I and II show mean coherence values of the power spectra between the HRV and VRV series in LF and HF bands. The model was applied using criteria of a mean coherence value higher than 0.5.

\[
\text{III. RESULTS}
\]

Results are presented as mean ± SD. Wilcoxon tests were used to determine the significance of the differences between rest and tilt, and between populations. A \( p < 0.05 \) is considered significant.

\[
\text{A. Spectral Analysis}
\]

The \( L_{\text{HF}}/L_{\text{HF}} \) and \( L_{\text{HF}}/L_{\text{HF}} \) values are
shown in tables III and IV for protocols I and II respectively.

**TABLE III**

<table>
<thead>
<tr>
<th>Subject</th>
<th>LF/(LF+HF)$_{HRV}$</th>
<th>LF/(LF+HF)$_{VRV}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swimmers</td>
<td>0.49±0.23</td>
<td>0.74±0.18</td>
</tr>
<tr>
<td>Judokas</td>
<td>0.49±0.23</td>
<td>0.84±0.11</td>
</tr>
<tr>
<td>Sedentary</td>
<td>0.52±0.16</td>
<td>0.68±0.22</td>
</tr>
</tbody>
</table>

**TABLE IV**

<table>
<thead>
<tr>
<th>Subject</th>
<th>LF/(LF+HF)$_{HRV}$</th>
<th>LF/(LF+HF)$_{VRV}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>0.46±0.29</td>
<td>0.54±0.29</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.45±0.17</td>
<td>0.59±0.13</td>
</tr>
<tr>
<td>Normal Subjects</td>
<td>0.68±0.16</td>
<td>0.80±0.09</td>
</tr>
</tbody>
</table>

**Fig. 2.** Examples of: (a) HRV sequences, (b) VRV sequences, (c) HRV power spectra, and (d) VRV power spectra for a normal subject in resting position.

**Fig. 3.** Examples of: (a) HRV sequences, (b) VRV sequences, (c) HRV power spectra, and (d) VRV power spectra for a cardiac transplant patient in resting position.

Both protocols and for all populations. In the case of LF/(LF+HF)$_{VRV}$ no significant changes were observed. Also, in protocol II, LF/(LF+HF)$_{HRV}$ allows to differentiate between populations, it is larger in control subjects than in heart failure patients ($p<0.01$) (see table IV).

Figure 2 shows HRV and VRV sequences and power spectra for a normal subject resting position. Both power spectra confirmed that the HRV and VRV series exhibit LF peaks.

Figure 3 shows HRV and VRV sequences and power spectra for a transplant cardiac patient in resting position. VRV spectrum is characterized by prominent HF peak, LF component is minor.

**B. Parametric Model**

Results of LF/(LF+HF) values from the parametric model for protocols I and II are summarized in tables V and VI, respectively.

**TABLE V**

<table>
<thead>
<tr>
<th>Subject</th>
<th>LF/(LF+HF)$_{VRV}$</th>
<th>LF/(LF+HF)$_{VRVu}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swimmers</td>
<td>0.59±0.22</td>
<td>0.66±0.29</td>
</tr>
<tr>
<td>Judokas</td>
<td>0.59±0.21</td>
<td>0.76±0.18</td>
</tr>
<tr>
<td>Sedentary</td>
<td>0.53±0.19</td>
<td>0.56±0.2</td>
</tr>
</tbody>
</table>

**TABLE VI**

<table>
<thead>
<tr>
<th>Subject</th>
<th>LF/(LF+HF)$_{VRV}$</th>
<th>LF/(LF+HF)$_{VRVu}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac transplant</td>
<td>0.31±0.25</td>
<td>0.33±0.27</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.31±0.22</td>
<td>0.36±0.27</td>
</tr>
<tr>
<td>Normal Subjects</td>
<td>0.47±0.28</td>
<td>0.57±0.23</td>
</tr>
</tbody>
</table>

No differences were observed neither in LF/(LF+HF)$_{VRV}$, nor in LF/(LF+HF)$_{VRVu}$ when subjects changed from rest to tilt ($p>0.05$).
Figures 4 and 5 show the VRV decomposition: VRVs, VRVu series and power spectra, for a normal subject and a cardiac patient respectively. For both, cases VRVs is more important, VRVu seems to be negligible. Both power spectra are characterized by an important HF peak.

![Decomposition of the VRV for a cardiac transplanted patient](image)

Fig. 5. Decomposition of the VRV for a cardiac transplanted patient: (a) VRVs series, (b) VRVu series, (c) VRV, power spectra, and (d) VRVu power spectra.

IV. DISCUSSION

The LF/(LF+HF)_HRV has been proposed as an index to evaluate ANS condition. Results of this work confirm this fact as the LF/(LF+HF)_HRV index provided significant differences between rest and tilt in four different ANS profiles: athlete subjects, cardiac transplant patients, heart failure patients, and normal subjects.

On the other hand, LF/(LF+HF)_VRV is not a marker of sympathovagal balance. In VRVr, we expected to find discriminant potential of LF/(LF+HF)_VRV, nevertheless, the dynamic decomposition did not reflect ANS balance. In VRVs and VRVu series, similar results for LF/(LF+HF) were observed, but this index did not allow to separate between rest and tilt test. This behavior could be explained as follows: i) the fact that ventricular repolarization depends on heart rate and ANS, but also on humoral factors that are not taken into account in the parametric model. ii) HF oscillations in VRV series is not yet a fully understood issue. Porta et al. [4] concluded that VRVu has its most important frequency components in the very low frequency band (VLF) and Wong et al. [3], reported that HF in VRV series has not physiological significance correlated to ANS regulation.

An important HF rhythm was observed in VRV sequences for all populations. This might explain the reversal power distribution between HRV and VRV, and stressed the difficulty of the interpretation of the physiological significance of LF/(LF+HF) in VRV series. HF component could reflect the mechanical effect of respiration. Since in cardiac transplant patients, ANS efferent nerves are severed during the surgical procedure, respiration seems to be the most important physiological source of HF component.

Low values of coherence observed in cardiac transplant patients show that the modulation of heart rate on ventricular repolarization is very low in this population. Control subjects must have a higher sensitivity of sinus node response to ANS than cardiac transplanted patients; however, non differences were found between these populations. This is because the large variance observed in cardiac transplant patient parameters. This variance is explained by the heterogeneous elapsed time after transplantation (60 ± 48 month) for this group.

Our findings are in agreement with previous studies [2, 3, 4, 11]. Where they have shown that most of the ventricular repolarization variability is due to the modulation of heart rate variability, LF components have better correlation than HF components (see tables I and II) and HF in VRV series reflects non neural mechanisms.

The model used in this work was proposed in the literature, nevertheless other techniques like standard prediction error tools would have been interesting to study.

Further research is needed to better understand repolarization ventricular phenomena. Adaptive identification modeling techniques is proposed as a step forward to explore VLF, LF and HF components.

REFERENCES