Using the Heart Rate Variability for classifying patients with and without Chronic Heart Failure and Periodic Breathing

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Abstract
Assessment of the dynamic interactions between cardiovascular signals can provide valuable information that improves the understanding of cardiovascular control. Heart rate variability (HRV) analysis is known to provide information about the autonomic heart rate modulation mechanism. Using the HRV signal, we aimed to obtain parameters for classifying patients with and without chronic heart failure (CHF), and with periodic breathing (PB), non-periodic breathing (nPB), and Cheyne-Stokes respiration (CSR) patterns. An electrocardiogram (ECG) and a respiratory flow signal were recorded in 36 elderly patients: 18 patients with CHF and 18 patients without CHF. According to the clinical criteria, the patients were classified into the follow groups: 19 patients with nPB pattern, 7 with PB pattern, 4 with Cheyne-Stokes respiration (CSR), and 6 non-classified patients (problems with respiratory signal). From the HRV signal, parameters in the time and frequency domain were calculated. Frequency domain parameters were the most discriminant in comparisons of patients with and without CHF: PTOT, PLF and fpHF. For the comparison of the nPB vs CSR patients groups, the best parameters were RMSSD and SDSD. Therefore, the parameters appear to be suitable for enhanced diagnosis of decompensated CHF patients and the possibility of developed periodic breathing and a CSR pattern.

Keywords: Chronic Heart Failure, Heart Rate Variability, Periodic Breathing.

1. Introduction

The elderly population is increasing, resulting in a concomitant increase in chronic diseases and functional impairment. Moreover, many elderly persons suffer from comorbid conditions and disabilities that can make it more difficult to determine the adequate treatment [1]. Some of the most common clinical problems in elderly patients are related to diseases of the cardiac and respiratory systems.

Elderly patients often develop breathing abnormalities, such as a periodic breathing (PB) pattern and Cheyne-Stokes respiration (CSR), which may be related with chronic heart failure (CHF). CHF is associated with major abnormalities of autonomic cardiovascular control, and is characterized by enhanced sympathetic nerve activity and cardiorespiratory disarrangement [2, 3]. PB is a breathing abnormality associated with various oscillatory forms characterized by rises and falls in ventilation, and CSR is a more severe form of a PB pattern in which apneas and hypopneas alternate with repetitive gradual increases and subsequent gradual decreases in ventilation [4]. PB has a prevalence as high as 70% in CHF patients [5], and is associated with increased mortality [6], especially in CSR patients [7]. Clinical studies show that elderly patients often have an altered breathing pattern, with PB and CSR, coinciding simultaneously with the presence or absence of CHF [8].

Heart rate variability (HRV) analysis provides a noninvasive tool that assesses changes in the autonomic nervous system and the sympatho-vagal balance [9–11]. As HRV is heavily influenced by respiration, in particular during rest, its interpretation remains difficult without concurrent assessment of breathing. HRV has been related to respiration, baroreflexes, and thermal regulation. These factors are reflected in spectral analysis studies of HRV. The high frequency (HF) component is considered a marker of parasympathetic activity, and is synchronous with respiration, whilst the low frequency (LF) component is a marker of sympathetic modulation, at least when measured in normalized units. However, the mechanisms that modulate the very low frequency (VLF) component are more controversial. They have been linked with humoral and temperature regulation, with slow vasomotor activity or with parasympathetic outflow [12]. In our previous study, we researched the oscillatory breathing pattern in elderly patients, using relevant information from the envelope respiratory pattern [13]. The aim of this study was to analyze heart rate variability (HRV) in elderly patients with and without chronic heart failure (CHF), and with a periodic (PB & CSR) or non-periodic (nPB) breathing pattern. An increase in our knowledge of the physiological condition of these patients could help to improve their diagnosis and prognosis.

2. Database

Electrocardiogram (ECG) lead I, and the respiratory flow signals were recorded in 36 elderly patients admitted to the short–stay unit (21 males, 15 females, aged 82_5 years) at the Santa Creu i Sant Pau Hospital in Barcelona, Spain. All subjects were studied according to a protocol previously approved by the local ethics committee (Ref. IIBSP-VEN-2012-168). The respiratory flow signal was acquired using a pneumotachograph connected to a mask (Neumotachometer Fleisch F3 - Honeywell 176 PC).

Prior to data acquisition, the patients were allowed to adapt for a few minutes so that they could feel comfortable with the mask. Respiratory flow signals were acquired for 15 min. All subjects were seated and remained awake throughout the acquisition (Figure 1).

Figure 1. *Signal acquisition process. Patient remained seated and awake throughout the acquisition.*

The signals were recorded at 250 Hz sampling rate. According to the clinical diagnosis, the patients were classified into two groups: 18 patients with CHF and 18 without CHF disease. After recording the respiratory flow signal, and according to the clinical criteria, the patients were also classified into the following three groups: 19 patients with non-periodic breathing (nPB), 7 patients with periodic breathing (PB), and 4 patients with a Cheyne-Stokes respiration (CSR) pattern. The remaining 6 patients were excluded from the study due to problems with the respiratory records. The same patient might present a mixture of breathing patterns, ranging from normal breathing (with no cyclic modulation of ventilation) through mild PB to CSR patterns.

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3. Methods

3.1. Signal processing

The respiratory flow signal was preprocessed to reduce artifacts. First, outlier samples below or above the threshold were removed. The threshold was taken as the mean of the signal ± 3 standard deviation. Next, short-duration spikes were removed using an auxiliary filtered signal, obtained as the original flow signal downsampled to 25 Hz and filtered by a median filter of order 11. Thus, samples for which the difference between the downsampled original signal and the auxiliary signal exceeded a threshold (set to half the standard deviation of the signal) were replaced by the median value of neighboring samples. Finally, considering that respiratory frequency normally ranges from 0.2 to 0.4 Hz and modulation frequency from 0.01 to 0.04 Hz, the signal was downsampled to 1 Hz.

The ECG was preprocessed to reduce artifacts. Wavelet techniques (Daubechies level 8) were applied to detrend and denoise procedures. The first technique removed the last detail level (Figure 2), and the second one used an adaptive threshold in each detail level (Figure 3) [14].

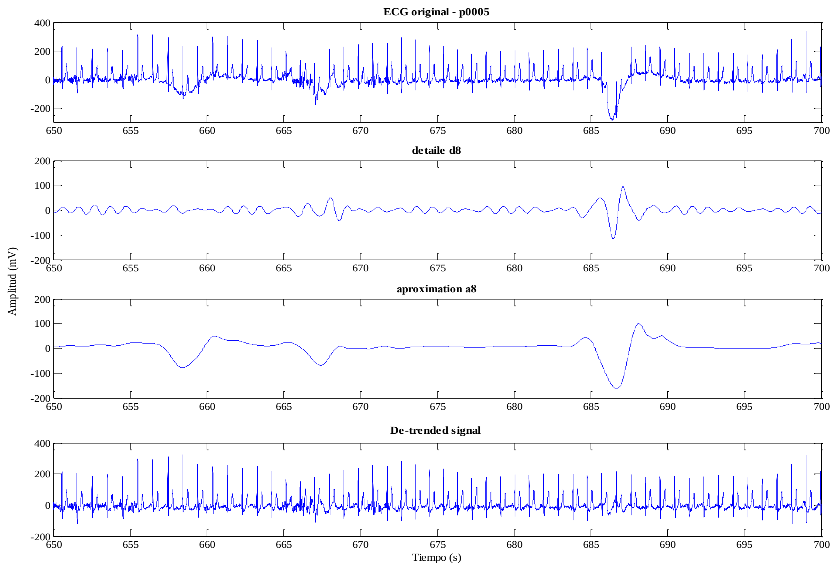

Figure 2. *Detrend process for ECG signal using Wavelet decomposition.*

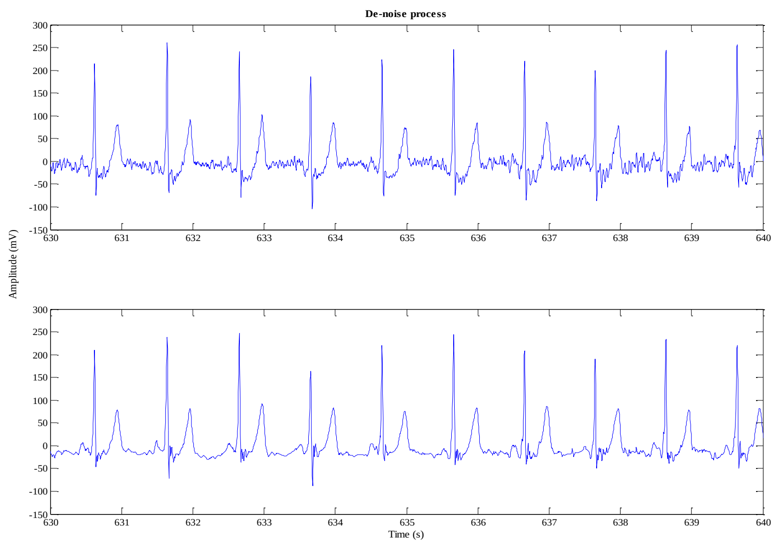

Figure 3. *Denoise process for ECG signal using an adaptive threshold.*

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3.2. Heart Rate variability

Heart rate time series consisting of beat-to-beat intervals (RR intervals) were extracted automatically from the ECG signal using an algorithm based on wavelet analysis [14]. Ectopic beats were determined, removed, and interpolated using an algorithm based on local variance estimation. The HRV signal was derived from the RR interval following a method based on the Integral Pulse Frequency Modulation model [15].

3.2. Parameter extraction.

HRV was characterized using time and frequency domain measures. In the time domain, according to [10], the follow parameters were calculated: SDNN (the average of the standard deviations of NN intervals for each 5 min segment), SDANN (standard deviation of the averages of NN intervals for each 5 min segment), RMSSD (the square root of the mean of the sum of the squares of differences between adjacent NN intervals), and SDSD (standard deviation of differences between adjacent NN intervals).

In the frequency domain, the power spectral densities of HRV were estimated using the modified covariance method, and were characterized on different spectral bands: total power (PTOT: 0–0.4 Hz), very low frequency (VLF: 0–0.04 Hz), low frequency (LF: 0.04–0.15 Hz), and high frequency (HF: 0.15–0.4 Hz). Table 1 shows the parameters extracted in the frequency domain.

Table 1. *Frequency parameters of HRV.*

Parameter	Units	Description
PVLF	dB	Power in band of VLF
PLF	dB	Power in band of LF
PHF	dB	Power in band of HF
LF/HF	dB	Power ratio between LF and HF
PTOT	dB	Power band of LF + HF
PLFnorm	dB	Normalized power in LF
PHFnorm	dB	Normalized power in HF
fpVLF	Hz	Frequency peak of PVLF
fpLF	Hz	Frequency peak of PLF
fpHF	Hz	Frequency peak of PHF

The statistical analysis was carried out using the SPSS program. The differences between the groups were tested by the Kolmogorov-Smirnov test. A p-value < 0.05 was considered significant.

4. Results

Table 2 presents the statistically significant p-values of the most relevant parameters obtained when the groups were compared.

Table 2. *p-value of the most significant parameters for each classification, calculated using the Kolmogorov-Smirnov Test.*

Parameter	CHF vs nCHF	nPB vs CSR	PB vs CSR
Statistical parameters			
SDANN	-	-	0.012
SDNN	0.050	-	0.002
RMSSD	-	0.028	0.001
SDSD	-	0.028	0.001
Frequency parameters			
PLF	0.022	-	-
PHFnorm	0.019	-	-
fpVLF	-	-	0.038
fpHF	0.021	-	0.032
LF/HF	0.037	-	-

The most discriminant parameters in the comparison of patients with and without CHF were in the frequency domain: PTOT *(p = 0.02)*, power of LF *(p = 0.022)*, frequency peak (*fp*) of HF *(p = 0.021)* and power ratio LF /HF *(p = 0.037)*. In the comparison of the nPB vs. the CSR groups, the best parameters were RMSSD *(p = 0.028)* and SDSD *(p = 0.028)*. No differences were obtained in the comparison of the nPB vs. the PB groups.

The performance of the HRV signal related to the respiratory flow signal was analyzed considering the amplitude of the respiratory flow signal for each beat, and the evolution of the beat per minute (BPM). Figures 4 and 5 show an example of these signals for a PB patient and a nPB patient, respectively. We observed that the evolution of BPM was more irregular in PB patients than in nPB patients.

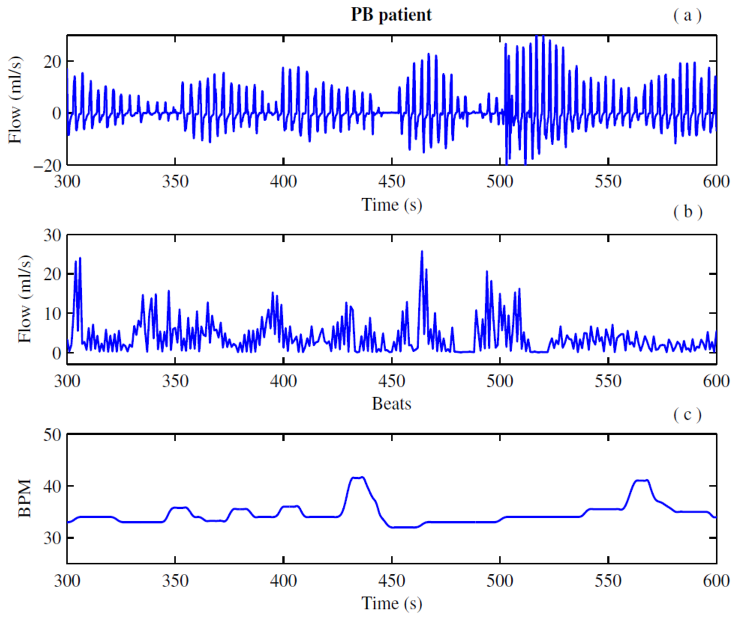

Figure 4. *(a) Respiratory Flow signal of a patient with a PB pattern, (b) amplitude of this respiratory flow signal for each beat, and (c) their BPM.*

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When we compared BPM in the nPB, PB, and CSR groups of patients, we found the greatest differences in the CSR group. The mean value of BPM was higher in CSR patients than in PB, and highest in nPB patients (see Figure 6).

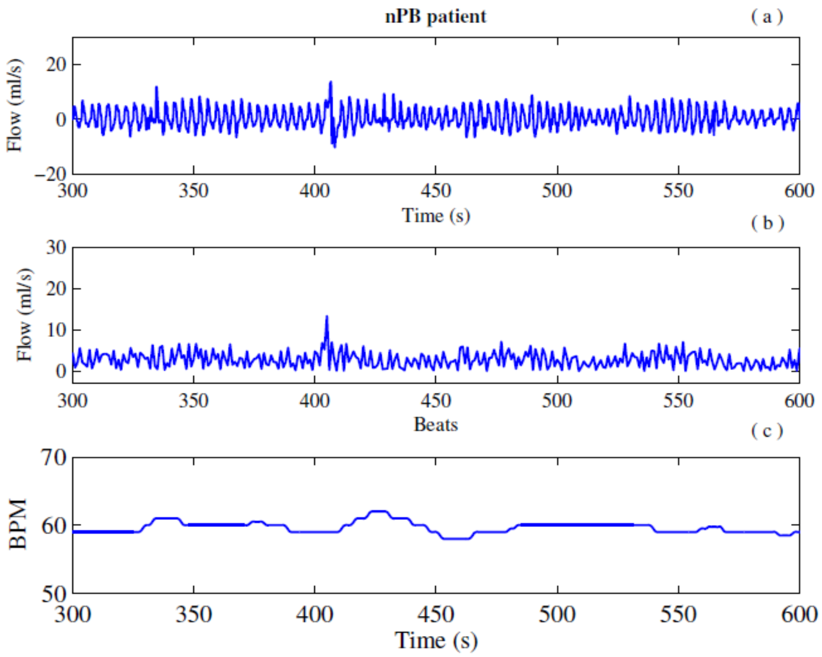

Figure 5. *(a) Respiratory Flow signal of a patient with a nPB pattern, (b) amplitude of this respiratory flow signal for each beat, and (c) their BPM.*

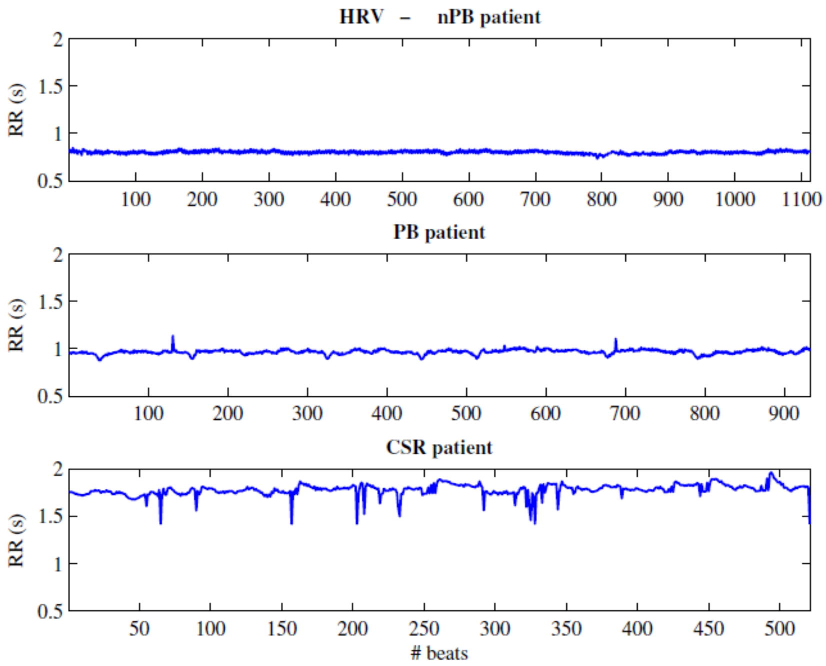

Figure 6. *Evolution of the BPM signal of a patient with (a) a non-periodic breathing pattern, (b) a periodic breathing pattern, and a Cheyne-Stokes respiration pattern.*

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5. Conclusion

In this study we researched the HRV signal to characterize patients with CHF and periodic breathing. Several parameters of the HRV frequency domain presented statistically significant differences in comparisons of patients with and without CHF disease.

The greatest differences in statistical parameters were obtained when PB and CSR patients were compared. In all cases, there were no differences in the comparisons of nPB and PB patients. We conclude that these parameters extracted from HRV might be another indicator for identifying patients with CHF. These parameters appear suitable for enhanced diagnosis of decompensated CHF patients, and the possibility of developing periodic breathing and CSR pattern.

With an increasing ageing population, early detection of a PB pattern could help to support and enhance the adequate diagnosis and treatment of diseases such as CHF, or to prevent these diseases, in elderly patients.

6. References

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