Characterization of Patients with Different Ventricular Ejection Fractions using Blood Pressure Signal Analysis

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Abstract

Ischemic and dilated cardiomyopathy are associated with disorders of myocardium. Using the blood pressure (BP) signal and the values of the ventricular ejection fraction, we obtained parameters for stratifying cardiomyopathy patients as low- and high-risk. We studied 48 cardiomyopathy patients characterized by NYHA $\geq$2: 19 patients with dilated cardiomyopathy (DCM) and 29 patients with ischemic cardiomyopathy (ICM). The left ventricular ejection fraction (LVEF) percentage was used to classify patients in low risk (LR: LVEF $> 35\%$, 17 patients) and high risk (HR: LVEF $\leq 35\%$, 31 patients) groups. From the BP signal, we extracted the upward systolic slope (BP_{sl}), the difference between systolic and diastolic BP (BPA), and systolic time intervals (STI). When we compared the LR and HR groups in the time domain analysis, the best parameters were standard deviation (SD) of $1/STI$, kurtosis (K) of BP_{sl}, and K of BPA. In the frequency domain analysis, very low frequency (VLF) and high frequency (HF) bands showed statistically significant differences in comaprisons of LR and HR groups. The area under the curve of power spectral density was the best parameter in all classifications, and particularly in the very-low- and high- frequency bands ($p < 0.001$). These parameters could help to improve the risk stratification of cardiomyopathy patients.

1. Introduction

Heart failure is a complex cardiovascular disease resulting from functional or structural cardiac disorders, mostly caused by coronary artery disease, hypertension and cardiomyopathy, and characterized by impaired ventricular filling or reduced left ventricular ejection fraction (LVEF) [1]. The problem in identifying cardiomyopathy patients who are at risk of sudden cardiac death (SCD) is still unsolved. The substrate for SCD varies depending on the underlying structural heart disease. Diseases predisposing to SCD include both hypertrophic cardiomyopathy and dilated cardiomyopathy [2]. Several studies have focused on the risk stratification of these patients [3–5]. However, in arrhythmia risk stratification, only LVEF was found to be a significant risk predictor in patients with idiopathic dilated cardiomyopathy, using multivariate analysis [6].

Conventionally, the evaluation of left ventricular (LV) systolic function is based on ejection fraction assessment, using the echocardographic technique. Various studies have aimed to obtain parameters such as systolic time intervals (STI) through conventional pulse Doppler echocardiography or tissue Doppler imaging to detect alterations in left ventricular function [7–9].

In this study, we analyzed the blood pressure (BP) signal of patients with dilated cardiomyopathy (DCM) and ischemic cardiomyopathy (ICM) for the noninvasive risk stratification of these patients. The aim was to obtain parameters (the time and frequency domain) from the blood pressure signal that can be used to characterize the behavior of patients with two different levels of LVEF: low and high risk.

2. Database

The non-invasive continuous blood pressure (BP) signal was recorded for 30 minutes from 48 cardiomyopathy patients, at the Santa Creu i Sant Pau Hospital in Barcelona, Spain. All patients were studied according to a protocol previously approved by the local ethics committee.

The recorded data was acquired with the Portapres-system (TNO Institute of Applied Physics, Amsterdam, Netherlands) and the Porti 16-biosignal amplifier (TMS International BV, Enschede, Netherlands). The patients characterized by NYHA ≥ 2 were classified into two groups: 19 patients with dilated cardiomyopathy (DCM) and 29 patients with ischemic cardiomyopathy (ICM). The left ventricular ejection fraction (LVEF) percentage was used to classify patients in low risk (LR: LVEF $> 35\%$, 17 patients) and high risk (HR: LVEF $\leq 35\%$, 31 patients) groups. Table 1 shows the clinical parameters of these patients.

Table 1. Clinical parameters

	LR	HR
Patients	17	31
DCM	6	13
ICM	11	18
Age [years]	62.6±12.9	66.0±9.5
Weight [kg]	75.3±15.1	82.3±16.1
BMI	27.2±3.8	29.0±5.1
NYHA	2.2±0.6	2.0±0.3
LVDD [mm]	56.4±6.5	63.7±5.9
Atrium Diameter [mm]	44.0±5.4	47.1±6.5
ProBNP	1086.3±956.5	1944.2±3154.2
LVEF [%]	43.3±8.8	28.7±5.2

DCM = dilated cardiomyopathy; ICM = ischemic cardiomyopathy; BMI = body mass index; NYHA = New York Heart Association functional classification; LVDD = left ventricular diastolic dysfunction; ProBNP = brain natriuretic peptide; LVEF = left ventricular ejection fraction.

3. Methods

3.1. Signal processing

The blood pressure signal was recorded at 1600 Hz, and re-sampled at 64 Hz. The linear trend was also removed.

The blood pressure signal is recorded using a finger cuff. Periods of constant cuff pressure are used to adjust the correct unloaded diameter of the finger artery, but the measurement of blood pressure is temporarily interrupted during such a period. When a study consider the dynamics of the signal over time, the cycles omitted by the calibration should be reconstructed. We reconstructed these cycles by considering the neighboring cycles before and after the calibration period. The original signal was adjusted in time to fit into the calibration segment, by cubic spline interpolation. The segment was then replaced by crossfading of the two extrapolated values, using the following window [10], [11]

$$w(n) = \begin{cases} 1 - \frac{1}{2}(2u(n))^{\alpha}, & u(n) \leq \frac{1}{2} \\ \frac{1}{2}(2 - 2u(n))^{\alpha}, & u(n) > \frac{1}{2} \end{cases} \quad (1)$$

where $u(n) = (n - n_s)/(n_e - n_s)$, and n_s and n_e are the indices of the onset and end of the calibration, respectively. Crossfading was carried out by multiplying the forward extrapolated sequence by $w(n)$ and the backward extrapolated sequence by $1-w(n)$. A linear down–slope was attained with $\alpha = 1$, whereas a step-like transition resulted when a $\alpha \to \infty$. The slope of the window was adjusted via the parameter $\alpha = 3$. Fig. 1 illustrates the process applied to this reconstruction.

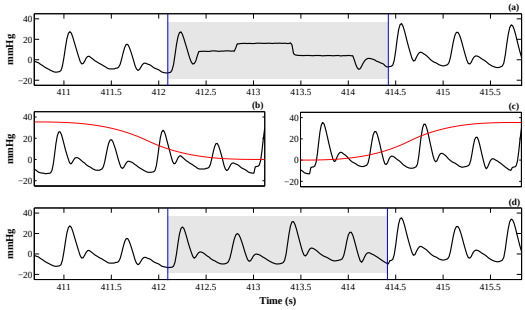

Figure 1. (a) Original blood pressure signal, (b) and (c) part of the signals before and after the calibration segment adjusted in time, where the cross-fade function is also shown, and (c) signal reconstructed without the calibration segment.

3.2. Characterization of blood pressure

The maximum value of the systolic pressure (SYS) for every heart beat was found by applying a slope sum function [12]. The pressure at the end of the diastole (DIA) was defined as the closest minimum before SYS.

Behavior of the blood pressure signal was characterized by systolic time intervals (STI) and defined as the time between successive SYS, the upward systole slope (BP_{sl}) between DIA and next SYS, the difference in amplitude between SYS and previews DIA (BPA), the time between the DIA and SYS (T_1), and the time between SYS and the end of the cardiac cycle (T_2). Figure 2 shows the time series extracted from the BP signal.

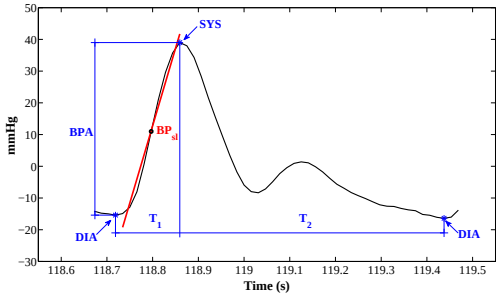

Figure 2. Characterization of the blood pressure signal.

Ectopic beats as well as other disturbances were removed. The time series were re-sampled at 4 Hz by applying a cubic spline function.

3.3. Spectral analysis

Power spectral densities (PSD) were estimated using the minimum variance distortionless response method (MVDR) [13], according to

$$\mathbf{S}_{xx}(\mathbf{F}) = \mathbf{F}^H \mathbf{R}_{xx} \mathbf{F} \quad (2)$$

being $\mathbf{R}_{xx}$ the covariance matrix of the input signal $\mathbf{x}(n) = [x(n)\ \ x(n-1)\ \ \ldots\ \ x(n-K+1)]^T$.

Fourier matrix $\mathbf{F} = [\mathbf{f}_0\ \ \mathbf{f}_1\ \ \ldots\ \ \mathbf{f}_{K-1}]$ is defined by

$$\mathbf{f}_k = \frac{1}{\sqrt{K}}[1\ \ exp(j\omega_k)\ \ \ldots\ \ exp(j\omega_k(K-1))]^T \quad (3)$$

where $\omega_k = 2\pi k/K$. Superscript *H* denotes the conjugate transpose matrix, and T the transpose.

Spectral signals were normalized by the total power of the signal. Figure 3 shows an example of $1/STI$, BP_{sl}, and BPA times series, and their PSD estimates.

3.4. Parameters extraction

The time series were characterized in the time and frequency domain by the parameters described in Table 2. The parameter extractions were performed in 4-minute segments, where the series were assumed to be stationary.

Table 2. Feature Description

Feature	Description
Time Domain	
M	mean value
SD	standard deviation
IQR	interquartile range
K	kurtosis
Frequency Domain	
P_p	Maximum peak of power
P_a	Area under curve of PSD
f_p	Frequency of P_p
P_{VLF}	Power in the band of VLF (0-0.04 Hz)
P_{LF}	Power in the band of LF (0.04-0.15 Hz)
P_{HF}	Power in the band of HF (0.15-0.4 Hz)
R_{LH}	Power ratio between LF and HF

4. Results

The groups LR and HR were similar in age, gender, BMI and NYHA. Table 3 shows the statistically significant parameters when LR and HR groups were compared. In the time domain analysis, the best parameters were SD of $1/STI$ ($p = 0.003$), K of BP_{sl} ($p = 0.002$), and K of BPA ($p < 0.001$).

Comparisons of LR and HR in the DCM patient group showed that the best parameters were IQR of BP_{sl} ($p = 0.004$) and SD of BPA ($p < 0.001$). The same parameters were the most significant in the ICM patient group.

The best results were obtained with the parameters of the frequency domain analysis. The VLF and HF bands showed statistically significant differences in comparisons of the LR and HR groups (see Table 3). Considering each group, DCM and ICM, P_a of VLF and HF were the best parameters in all cases, in comparisons of LR and HR ($p < 0.001$).

5. Conclusion

In this study we researched the blood pressure signal to stratify risk for patients with cardiomyopathy disease.

Table 3. Time and frequency parameters of blood pressure signal when comparing LR vs. HR groups, presented as mean and 95% confidence interval.

	LR	HR	*p*-value
Features $1/STI$			
M [1/s]	1.08 (1.03-1.12)	1.15 (1.11-1.19)	0.027
SD [1/s]	0.06 (0.05-0.07)	0.07 (0.06-0.07)	0.003
IQR	0.06 (0.05-0.07)	0.08 (0.07-0.09)	0.028
P_p [nu]	15.19 (13.53-16.85)	14.13 (12.50-15.75)	0.005
f_p [Hz]	0.075 (0.05-0.10)	0.11 (0.09-0.13)	0.002
P_aVLF [nu]	0.25 (0.23-0.28)	0.18 (0.16-0.20)	<0.001
P_aLF [nu]	0.35 (0.32-0.37)	0.31 (0.29-0.32)	0.012
P_aHF [nu]	0.38 (0.35-0.42)	0.49 (0.46-0.51)	<0.001
R_{LH}	1.33 (1.14-1.52)	0.91 (0.79-1.03)	<0.001
Features BP_{sl}			
M [mmHg/s]	8.65 (8.11-9.19)	9.60 (9.05-10.13)	0.018
K	3.29 (2.93-3.75)	3.47 (3.25-3.69)	0.002
P_p [nu]	30.46 (27.44-33.47)	19.46 (17.48-21.44)	<0.001
P_aVLF [nu]	0.47 (0.43-0.51)	0.28 (0.26-0.31)	<0.001
P_aHF [nu]	0.28 (0.25-0.31)	0.46 (0.44-0.48)	<0.001
R_{LH}	1.23 (1.06-1.39)	0.60 (0.54-0.66)	<0.001
Features BPA			
K	3.23 (2.71-3.74)	3.75 (3.39-4.12)	<0.001
P_p [nu]	33.70 (30.63-36.76)	23.65 (21.57-25.73)	<0.001
P_aVLF [nu]	0.51 (0.47-0.55)	0.33 (0.31-0.36)	<0.001
P_aHF [nu]	0.26 (0.23-0.29)	0.42 (0.40-0.45)	<0.001
R_{LH}	1.28 (1.11-1.46)	0.71 (0.62-0.80)	<0.001

nu = normalized units.

When linear time and frequency domain methods were applied to blood pressure time series, significant differences became apparent between high- and low-risk cardiomyopathy patients. In particular, the variability of the systolic time interval, the blood pressure amplitude, and the upward slope of the systole as a marker of altered complexity within the time series increased with the progression of disease. The power-related parameters allowed the best discrimination with the frequency method, especially in the very-low- and high- frequency bands, in all classifications. One limitation of this study is the low number of patients in both analyzed groups.

To conclude, this study suggests that easily calculable linear indexes from systolic and diastolic blood pressure, along with traditional clinical indexes (such as LVEF and NYHA), could improve the identification of low- and high-risk cardiomyopathy patients, therefore contributing to early noninvasive prediction of sudden death.

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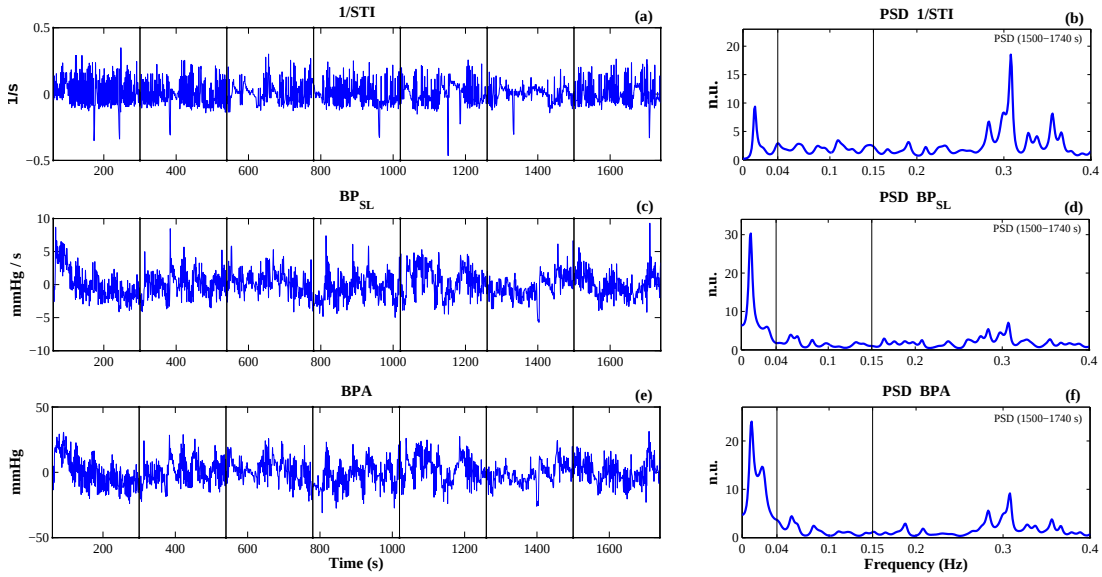

Figure 3. Time series and PSD of (a) and (b) inverse of systolic time interval, (c) and (d) systolic blood pressure slope, and (e) and (f) blood pressure amplitude.

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