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Classification of ischemic and dilated cardiomyopathy patients based on the analysis of the pulse transit time

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***Abstract*— Cardiomyopathies diseases affects a great number of the elderly population. An adequate identification of the etiology of a cardiomyopathy patient is still a challenge. The aim of this study was to classify patients by their etiology in function of indexes extracted from the characterization of the pulse transit time (PTT). This time series represents the time taken by the pulse pressure to propagate through the length of the arterial tree and corresponding to the time between R peak of ECG and the mid-point of the diastolic to systolic slope in the blood pressure signal. For each patient, the PTT time series was extracted. Thirty cardiomyopathy patients (CMP) classified as ischemic (ICM – 15 patients) and dilated (DCM – 15 patients) were analyzed. Forty-three healthy subjects (CON) were used as a reference. The PTT time series was characterized through statistical descriptive indices and the joint symbolic dynamics method. The best indices were used to build support vector machine models. The optimal model to classify ICM versus DCM patients achieved 89.6% accuracy, 78.5% sensitivity, and 100% specificity. When comparing CMP patients and CON subjects, the best model achieved 91.3% accuracy, 91.3% sensitivity, and 88.3% specificity. Our results suggests a significantly lower pulse transit time in ischemic patients.**

***Clinical relevance*— This study analyzed the suitability of the pulse transit time for the classification of ICM and DCM patients.**

I. Introduction

Diseases like cardiomyopathies affect a large part of the elderly population. Clinically differentiation between several types of them are still challenging. For instance, the ischemic cardiomyopathy (ICM) and dilated cardiomyopathy (DCM) patients present similar symptoms, despite the differences in their etiology. The analysis of systems related to their pathological behaviour could help to differentiate between these cardiomyopathies and contribute to improve earlier diagnosis of these patients [1, 2].

Several linear and non-linear techniques based on the analysis of biomedical signals have been applied to study differences between cardiomyopathies patients [3-5]. Some differences between ICM and DCM patients have been presented in function of their biochemical processes [6, 7]. Another study showed an abnormal regulation of contractility in in dilated hearts, analyzing their mechanical behaviour [8].

One way to study the behaviour of cardiomyopathies through ECG, blood pressure and respiratory flow signals is by analyzing the interactions between their physiological systems. In our previous work, we explored the interactions between the cardiac and respiratory systems in function of the changes in blood pressure and found respiratory patterns that were characteristic of dilated cardiomyopathy patients [9].

In this work, we propose the analysis of the same patients considering the relation between each heartbeat and each blood pressure pulse, through the pulse transit time (PTT). This time series represent the length of time it takes for the pulse pressure to propagate through the length of the arterial tree. This index allows to study the relations between electrical activity of the heart and the pump capacity of cardiac muscle through the electrocardiographic and blood pressure signals, respectively. The main objective of this study is to analyze the suitability of the PTT to classify patients by their etiology. We propose to characterize these time series using statistical parameters and the joint symbolic dynamics method.

II. Database

The non-invasive electrocardiographic (ECG) and blood pressure (BP) recordings from 30 cardiomyopathy patients were registered at the Santa Creu I Sant Pau Hospital, Barcelona, Spain. Every recording was performed according to a protocol, approved by the Hospital ethics committee. The patients were characterized by the New York Heart Association function (NYHA) ≥ 2 and were diagnosed by either ischemic cardiomyopathy (ICM – 15 patients) or dilated cardiomyopathy (DCM – 15 patients). Forty-three healthy subjects were used as a reference (CON). Table I summarizes the clinical information of these patients.

The recordings were acquired with the Portapres-system and the Porti 16-biosignal amplifier, for 15 minutes, at a sample frequency of 1600 Hz, with the patient in supine position [9].

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TABLE I. CLINICAL INDICES

	ICM	DCM
Patients	15	15
Age [years]	65.4 ± 11.9	61.7 ±12.9
Weight [kg]	81.4 ± 13.3	81.3 ± 17.9
BMI [kg/m^2]	28.1 ± 3.4	28.7 ± 6.6
NYHA	2.1 ± 0.3	2.1 ± 0.7
LVDD [mm]	63.7 ± 8.6	67.8 ± 4.2
AD [mm]	47.3 ± 8.3	44.7 ± 4.1
ProBNP	1327.1 ± 1458.6	1131.2 ± 1835.6
LVEF [%]	33.0 ± 6.9	37.5 ± 6.2

BMI = Body Mass Index; NYHA = New York Heart Association functional classification; LVDD = Left Ventricular Diastolic Dimension; AD = Auricular Diameter; ProBNP = Brain Natriuretic Peptide; LVEF = Left Ventricular Ejection Fraction.

The ECG and BP signals linear trend were removed, and in-house preprocessing tools were used to reduce noise, artifacts, and spikes. All outliers were eliminated.

III. METHODOLOGY

A. Signal Processing

The time series of the pulse transit time (PTT, [ms]) was extracted from the ECG and BP signals using an in-house algorithm considering the time elapsed between the R peaks and the mid-point of the rise of the corresponding blood pressure pulse for each heartbeat. Thereafter, the series were inspected and edited, if necessary. Fig 1. Shows an example of the pulse transit time.

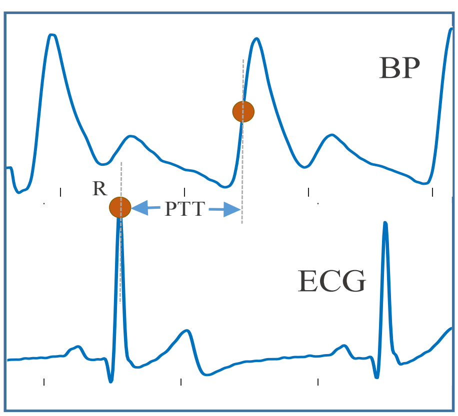

Figure 1. Example of the pulse transit time.

B. Statistical characterization

The PTT time series was characterized through statistical descriptive indices that includes the mean (PTT_m), standard deviation (PTT_{sd}), kurtosis (PTT_K), skewness (PTT_{Sk}), interquartile range (PTT_{IQR}), and coefficient of variation (PTT_{CV}).

C. Joint symbolic dynamics

The joint symbolic dynamics (JSD) characterization method is useful to quantify the non-linear behavior of a time series by the means of symbols [10]. We transformed the PTT series using a symbolic alphabet {0, 1}, according to:

$$S_n^{PTT} \begin{cases} 0: (PTT_{n+1} - PTT_n) \leq 0 \\ 1: (PTT_{n+1} - PTT_n) > 0 \end{cases} \quad (1)$$

We defined a word as a sequence of three consecutive and non-overlapping symbols. A vector W_n^{PTT} was constructed containing all word iterations from [000] to [111]. Finally, the probability of occurrence of each word was assessed and analyzed considering $pPTT_w$. Table II shows a summary of the indices considered.

TABLE II. INDEX DESCRIPTION: STAITSTICAL AND PROBABILITY OF OCURRENCE OF WORDS

Statistical	***Description***
PTT_m	PTT mean value
$\boldsymbol{PTT_{sd}}$	$\boldsymbol{PTT}$ standard deviation
$\boldsymbol{PTT_K}$	$\boldsymbol{PTT}$ kurtosis
PTT_{Sk}	PTT skewness
PTT_{CV}	PTT coefficient of variation
$\boldsymbol{PTT_{IQR}}$	$\boldsymbol{PTT}$ interquartile range
JSD	***Description***
$pPTT_{000}$	word 000
$pPTT_{001}$	word 001
$pPTT_{010}$	word 010
$pPTT_{011}$	word 011
$pPTT_{100}$	word 100
$pPTT_{101}$	word 101
$pPTT_{110}$	word 110
$pPTT_{111}$	word 111

D. Classification

The support vector machines (SVM) method is useful for classification tasks where the classes are not linearly separable in the original space. By transforming the data into a higher dimensional space, SVM aims to solve a simple linear problem instead of the originally complex non-linear one. This process is achieved through the optimization of a hyperplane defined by the SVM function, being $X = \{x_1, \dots, x_L \in \mathbb{R}\}$ for a given set of data vectors and $Y = \{y_1, \dots, y_L\}$ their corresponding labels.

$$f(x) = wz + b = \sum_i^L \alpha_i y_i K(x_i y_i) + b. \quad (2)$$

The $K(x_i y_i)$ term is known as the Kernel function that shapes the hyperplane and α_i and b define the efficiency of the classifier on optimal conditions [11]. From all the possible Kernel types we evaluated the Gaussian, Laplace and ANOVA.

The Gaussian Kernel is often used to model radially distributed data,

$$K(x,y) = e^{-\left(\frac{\|x-y\|^2}{2\sigma^2}\right)} \quad (3)$$

were σ is a penalization term.

The Laplace kernel is a less σ influenced version of the Gaussian kernel,

$$K(x,y) = e^{-\left(\frac{\|x-y\|^2}{2\sigma}\right)}. \quad (4)$$

The ANOVA kernel is used on multidimensional support vector regression models,

$$K(x,y) = \sum_{k=1}^{n} e^{\left(-\sigma\left(x^k-y^k\right)^2\right)^d} \quad (5)$$

being σ and d the optimization indices.

The classification problem is then solved by maximizing the margin while minimizing the training error. Using the Lagrange multipliers method, a dual formulation is obtained,

$$minP(w,b) = \frac{1}{2}\|w_m z\|^2 + C\sum_i K_1[y_i f(x_i)] \quad (6)$$

were C is a penalty parameter. Despite C having no direct meaning, when its value increases, the penalty assigned to errors is stronger, narrowing the decision boundary.

Each feature was scaled and normalized (zero mean and unit variance) in order to avoid scaling biases. For each iteration of features, the model was built by optimizing the value of C for each of the kernels considered, by iterating different values of σ and d.

The indices that showed statistical differences and low correlation were used in pairs to build several SVM models. The specificity and the accuracy of each model was calculated and the one with the higher value (specificity then accuracy) was chosen as optimal for each type of kernel.

A. *Statistical Analysis*

A Kolmogorov-Smirnov non-parametric statistical test was applied to evaluate the statistical significance of the indices, with *p*-value ≤ 0.05. In addition, a correlation analysis was performed on those indices that presented statistically significant differences. For highly correlated indices ($\rho \geq 0.7$), the one with the lowest statistical significance was discarded. The leave-one-out cross-validation was used to validate the results, who are presented in terms of accuracy (*Acc*), sensitivity (*Sn*), and specificity (*Sp*).

IV. RESULTS

A total of 14 indices were obtained during the characterization step. The results were studied considering two different comparisons:

- Ischemic vs dilated cardiomyopathy patients (ICM vs DCM)
- Cardiomyopathy patients vs Control (CMP vs CON)

When ICM and DCM patients were compared 4 indices shown statistically significant differences. One of them was correlated with another index with higher statistical power and was discarded. The remaining 3 indices were used for the classification task.

In the analysis of CMP patients and CON subjects 9 indices presented statistically significant differences. From these indices 2 presented high correlation with indices with higher statistical power and were discarded. The remaining 7 indices were used to build the classification models. Table III shows the most relevant indices for each comparison, expressed as mean value and standard deviation (SD).

TABLE III. SIGNIFICANT INDICES SUMMARY (MEAN ± SD): COMPARING ICM VERSUS DCM PATIENTS AND CMP PATIENTS VERSUS CON SUBJECTS

ICM vs DCM			
Index	**ICM (15)**	**DCM (15)**	**p-value**
$\boldsymbol{PTT_m}$	1.2 ± 0.7	4.1 ± 4.0	0.04
$\boldsymbol{PTT_{sd}}$	0.5 ± 0.3	2.2 ± 2.1	0.03
PTT_{IQR}	0.6 ± 0.5	3.9 ± 4.8	0.002
PTT_K	2.8 ± 4.3	-1.1 ± 0.4	<0.001
CMP vs CON			
Index	**CMP (30)**	**CON (43)**	**p-value**
PTT_m	2.9 ± 3.2	7.4 ± 6.4	<0.001
PTT_{sd}	1.6 ± 1.4	4.6 ± 4.5	<0.001
PTT_{IQR}	2.5 ± 3.6	7.9 ± 7.7	<0.001
PTT_K	0.24 ± 2.9	-0.9 ± 0.5	0.04
$pPTT_{001}$	0.1 ± 0.07	0.09 ± 0.05	0.009
$pPTT_{010}$	0.13 ± 0.09	0.03 ± 0.03	<0.001
$pPTT_{100}$	0.13 ± 0.05	0.08 ± 0.04	0.007
$pPTT_{101}$	0.1 ± 0.08	0.05 ± 0.04	0.01
$pPTT_{111}$	0.08 ± 0.06	0.41 ± 0.21	<0.001

The PTT_K and PTT_{IQR} were the optimal indices to make the ICM vs DCM model with Laplace kernel, achieving 89.6% accuracy, 78.5% sensitivity and 100% specificity. The CMP vs CON comparison model was built with the ANOVA kernel and the PTT_{sd} and $pPTT_{111}$, obtaining 91.3% accuracy, 94% sensitivity and 88.3% specificity. Table VI presents the classification results, and Fig 2. the SVM scoreplots results.

TABLE IV. CLASSIFICATION RESULTS

Groups	*C*	*σ*	*d*	*Acc(%)*	*Sn(%)*	*Sp(%)*
ICM vs DCM	1.2	0.7	-	89.6	78.5	100
CMP vs CON	2.5	0.2	1.2	91.3	91.3	88.3

C: Penalty parameter of SVM; σ and d: Penalization term of kernels; Acc: Accuracy; Sn; Sensitivity; Sp: Specificity

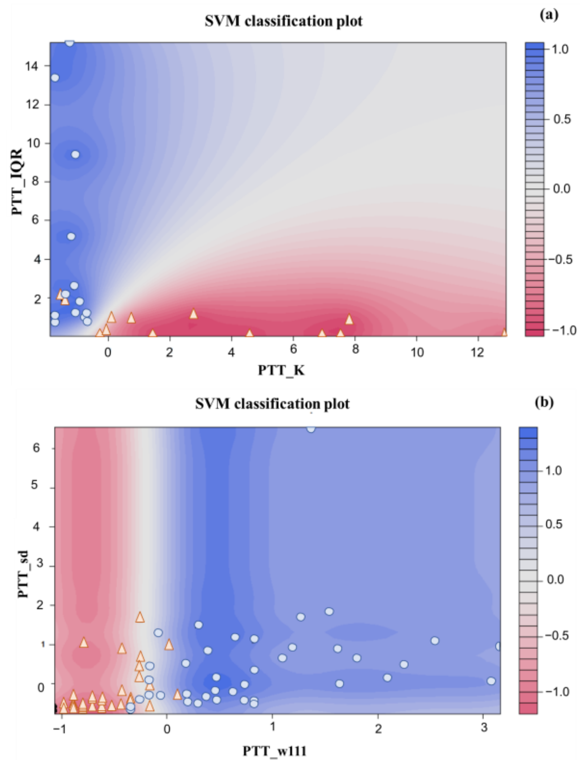

Figure 2. Support vector machine classification results. a) ICM (○) vs DCM (△), b) CMP (△) vs CON (○).

V. DISCUSSION AND CONCLUSION

The suitability of the analysis of the pulse transit time for the characterization and classification of cardiomyopathy patients was explored. The relevant indices extracted were used to classify the patients and control subjects.

Our results suggest that ICM patients showed lower PTT values than DCM patients and CON subjects, and with less dispersion. Previous studies also presented lower levels of PTT values in pathological conditions [12, 13]. On the other hand, ICM patients showed higher kurtosis values than DCM patients, suggesting a less stable behaviour than the one observed in DCM patients.

In comparison with the CON subjects, the patients showed lower PTT values on average, and with a more stable behaviour. We also observed that the increasing behavior ($p\mathrm{PTT}_{111}$) is less prevalent in pathological conditions. We hypothesize that these PTT increasing patterns, in CMP patients, is instead performed by smooth increasing patterns ($p\mathrm{PTT}_{001}$) with some alternant patterns ($p\mathrm{PTT}_{010}$, $p\mathrm{PTT}_{101}$), since these patterns are more prevalent in CMP patients in comparison with control group.

In conclusion, the analysis of the pulse transit time provided novel insight in the classification of cardiomyopathy patients. These results are promising in the characterization of cardiomyopathy patients by their etiology, especially ischemic cardiomyopathy patients. However, these results should be validated with a greater number of patients.

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