Chaos Theory and Non-linear Dynamics in Hypertensive Cardiopathy and Heart Failure

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Abstract. *Heart failure is worldwide cause for increased morbidity and mortality. High sympathetic activity is a potential factor for ventricular arrhythmias. Depressed heart rate variability (HRV) in heart failure is associated with increased mortality. Nonlinear analysis may quantify abnormalities in RR intervals series based on fractal analysis (chaos theory). Approximate entropy (ApEn) was applied to quantify the regularity and complexity of time series, as well as unpredictability of fluctuations in time series.*
Dynamic analysis based on chaos theory points out the multifractal time series in heart failure patients who loss normal fractal characteristics and regularity in HRV.
Hypertension is a risk factor for the development of heart failure (HF), both because hypertension increases cardiac work, which leads to the development of left ventricular hypertrophy, and because hypertension is a risk factor for the development of coronary heart disease. Knowing the role of the autonomic nervous system (ANS) in the mechanism of hypertension, the challenge is to evaluate the arrhythmic risk of hypertensive patients. Disturbances in the activity of the autonomic nervous system (ANS) also significantly influence the outcome of patients with chronic heart failure (CHF).
A subject open to debate is to compare heart rate variability (HRV) parameters and the chaos theory methods for the assessment of the clinical status and the outcome in hypertensive cardiopathy. Also we consider that it is necessary to improve ventricular arrhythmia prophylaxis in patients with preserved left ventricular left ejection fraction heart failure.

Keywords: Hypertension, heart failure, nonlinear analysis

1. Background

Rhythmic changes of blood pressure, heart rate, and other cardiovascular measures have drawn the attention of several investigators, since these oscillations can shed light onto the activity of the underlying control network [6].

Cardiovascular function is regulated by the autonomic nervous system (ANS). ANS is a neural network that operates at the subconscious level and regulates the visceral functions of the body. The main aim of autonomic cardiovascular regulation is to control cardiac output and the distribution of blood at the central and peripheral levels. Heart rate (HR) and the contractile properties of the myocardium, which contribute to cardiac output, are modulated by the main components of ANS: the parasympathetic and sympathetic nervous systems. The activity of these two ANS branches with opposite effects on HR causes continuous fluctuations in HR, which is called heart rate variability [3, 4].

Heart rate variability (HRV) has become a universal tool to study the neural control of the heart i.e. the delicate interaction between sympathetic and vagal influences on heart rate in health and disease. HRV can be quantified by the simple calculation of the mean and standard deviation of RR-intervals in the time domain. Furthermore, in the frequency domain, spectral analysis of HRV reveals two distinct frequency regions in the modulation of heart rate in humans. A high frequency region (0.15-0.4 Hz) which is a marker of vagal modulation, and a low frequency region (0.04-0.15 Hz), which reflects predominantly sympathetic tone andbaroreflex activity [2]. A variety of linear, non-linear, periodical and nonperiodical oscillation patterns are present in heart rate fluctuations [1].

Detrended fluctuation analysis (DFA) has been introduced to evaluate the fractal correlation properties of R-R interval dynamics and to characterize the features of HR dynamics that may not be easily detectable by traditional methods of analysis. Breakdown of fractal organization into beat-to-beat R-R interval dynamics indicates increased cardiac vulnerability and a higher risk of mortality in patients with and without structural heart disease [5].

Hypertension represents an important condition that affects the adult population worldwide; it contributes significantly to morbidity and mortality from stroke, heart failure, coronary heart disease and renal failure [7]. The sympatho-vagal balance is altered in the resting conditions of numerous pathophysiological processes. It is the case of essential arterial hypertension (Guzzetti et al. 1988), even in the presence of arterial pressure values still in the high normal range (Lucini et al. 2002). The ability of decreased heart rate variability to predict incident hypertension has not been well studied, and there are no studies of whether hypertension leads to changes in heart rate variability [8].

The purpose of this study was to assess the physiological basis of methods evaluating beat-to-beat R-R interval dynamics and to assess new methods in the evaluation of ventricular arrhythmia and sudden cardiac death in congestive heart failure patients [7]. Finding and analysing hidden dynamical structures of these signals are of basic and clinical interest [2].

2. Method

The study was performed at the Cardiology Clinic of the Emergency County Hospital Timis, University of Medicine and Pharmacy “V. Babes “Timisoara. The study group has included hypertensive patients (n: 47, men: 23, women: 24, mean age: 54.2 yrs.) with hypertension stage II and III WHO classification and patients (n: 61) with heart failure with history of ischaemic heart disease (mean age: 61.3 yrs., M: 42, W: 19).

ECG signal analysis and blood pressure measurements were done using a EC-3H/ABP Combined Holter System, Labtech Ltd. The system performs simultaneously recording of the ECG signal and measurements of the blood pressure.

Twenty four hours of combined ECG and blood pressure monitoring was performed and more than 90 % of the signals and measurements were eligible for the study. Artefacts and noise was manually removed from the signals.

All ECG analysed signals were in sinus rhythm and analysis of heart rate variability was performed in time domain, mean RR intervals (ms.), standard deviation of all RR intervals ms) and frequency domain, very low frequency (VLF, 0.01-0.05 Hz), low frequency (LF, 0.05 -0.15 Hz) and high frequency (HF, 0.15-0.50 Hz), LF/HF ratio. Kubios v. 2.1, Finland (http://kubios.uku.fi/) was used for the measurement of the nonlinear parameters of the RR series. Approximate Sample entropy, detrended fluctuation analysis, and Poincare plots, have been used for the study of the behaviour of the heart rate dynamics.

Trends of heart rate (b/min) and blood pressure (mmHg) were recorded. Left ventricular ejection fraction (LVEF, %) was measured echocardiographic by an independent member of the team.

All patients included in the study underwent noninvasive evaluation comprising a physical examination, 12-lead ECG, chest radiography, M-mode and B-mode echocardiography, and 24-h Holter ECG. Following the left ventricular ejection fraction (LVEF) below 45% and above 45% we subdivided the heart failure group in altered LVEF (< 45%) and preserved LVEF (> 45%) subgroups.

The mean of all RR intervals (NN), standard deviation of all normal–normal RR intervals (SDNN), the nonlinear dynamics parameters, as detrended fluctuation analysis short-term α1 (DFA α1), Poincaré plot analysis, and sample entropy analysis were performed for all ECG signals. From the Poincaré plot analysis, using Kubios HRV 2.0 software, we obtained automatically the values of the short-term scaling exponent (α1).

Spectral power was quantified by fast-Fourier transformation analysis (FFT 256 points, Welch) and by autoregressive method, model 20 in 2 frequency bands: low frequency (0.05 – 0.15 Hz) and high frequency (0.15 – 0.4 Hz). We quantified several time domain HRV parameters: mean HR, standard deviation of normal HR data (SDNN) and the spectral analysis was performed on linearly resampled (1 Hz) time series using Welch's method. The 256-point fast Fourier transform was repeatedly computed with 50% overlap between adjacent segments. [6]. Low-to-high frequency ratio was considered as marker of the autonomic tone.

3. Statistical analysis

For the statistical analysis we used Graph Pad Prism. All numeric variables were expressed as mean and the statistical analysis was performed using Student's t-test and correlation analysis by Pearson method. A p value < 0.05 was considered statistically significant.

4. Results

The characteristics of the study population are presented in Table 1.

Table 1 Characteristics of the study population

Parameters	LVEF > 45 %	LVEF < 45 %	Arrhythmia	Control
No patients	27	29	29	15
Male/Female	15 / 12	22 / 7	22 /7	8 / 7
Age (yrs.)	58.7	63.8	64.8	44.7
LVEF (%)	54.4	37.9	44.3	71.3
NYHA III-IV	12	23	24	0
NSVT	14	16	29	0

The mean age of the patients subgroup with altered LVEF (A) was significant lower compared with the mean age of patients subgroup with preserved LVEF (B), 58.7 vs 63.8 yrs., p<0.05. The patients subgroup with altered LVEF was characterized by a higher NYHA functional classes (NYHA III-IV, n: 23) compared to the patients subgroup with preserved LVEF (NYHA III-IV, n: 12). The LVEF was significant lower in subgroup A compared to subgroup B (54 % vs 38 %, p<0.001). The subgroup A had a higher incidence of ventricular arrhythmias compared to the subgroup B. The patients subgroup with altered LVEF had a lower heart rate compared to the patients subgroup with preserved LVEF (77 b/min vs 87 b/min), probably as a response to β-blockade, but significant higher compared to the control group.

The SDNN (ms) was significantly lower in the subgroup with altered LVEF when compared to the preserved LVEF group and to control (118 ms vs 141ms vs 167 ms, p < 0.001). A high sympathetic tone was noticed in the heart failure group compared to control, expressed as heart rate or LF/HF ratio (Table 2). Patients with altered LVEF had a high sympathetic tone characterized by a higher heart rate, high LF/HF ratio and depressed high frequency power spectrum density (figure 1). This was correlated with a higher incidence of ventricular arrhythmias.

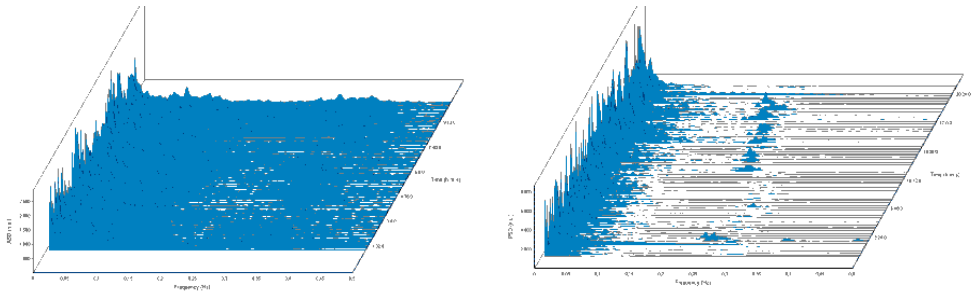


Fig. 1 Power spectral analysis in control group (a) and in the heart failure group (b)

The values of the nonlinear dynamic parameters, like DFA α1 and the Poincaré plots showed altered values (figure 2). DFA α1 was significant lower in the subgroup A compared to the entire heart failure group or to the control group (0.63 vs 0.97, $p < 0.001$).

Analysing the heart failure group, from the perspective of the presence or absence of acute coronary syndrome, we noticed that the most vulnerable patients group was characterized by high heart rate, high LF/HF ratio and low DFA α1, independently to the values of left ventricular ejection fraction (Table 2).

Table 2 HRV and Nonlinear dynamic parameters in heart failure group

	LVEF < 45 %	LVEF > 45 %	Heart Failure	Control Group
N	29	27	56	15
SDNN (ms)	118	141	128.9	167
Heart rate (b/min)	77	87	83.5	72.9
LVEF (%)	37.9	54.4	45.7	71.3
LF/HF	1.74	1.59	1.67	0.85
DFA α1	0.63	0.71	0.68	0.97
DFA α2	0.79	0.87	0.78	0.98
ApEN	0.97	1	0.96	1.21
SamEn	0.87	0.95	0.87	1.15

In the hypertensive group the gender distribution was almost equal, suggesting a higher incidence of essential hypertension in the women population and probably that the men were much earlier hypertensive than women. In the study group, women had mean age: 57 yrs. compared to men mean age: 50.4 yrs. ($p< 0.005$). Differences were noticed also in relation to the mean heart rate. Women were more tachycardic than the men hypertensive population (mean heart rate: 87 b/min vs. 80 b/min), but the differences were statistically significant. Considering only the gender aspects, in the hypertensive group, the left ventricular ejection fraction (LVEF %) seemed to be preserved, LVEF: 60 %, mean LVEF in the men population: 58 % compared to the women mean value: 61 %. In the hypertensive group, those with events had a lower left ventricular ejection compared with the events free hypertensive population (LVEF: 48 % vs. 68 %, $p< 0.005$). All the clinical data are resumed in Table 3.

Table 3 Main clinical characteristics of the hypertensive and the control group.

	Hypertension	Control	P

N	47	20	0.05
Age (yrs.)	54.2	46	0.05
Mean heart rate (b/min)	86	73	0.05
LVEF (%)	60	72	0.05
Systolic Blood Pressure (mmHg)	160	127	< 0.005
Diastolic Blood Pressure (mmHg)	105	75	< 0.005

Analysing the hypertensive group, we noticed differences between the dynamics of heart rate and systolic blood pressure as a measure of the circadian rhythm. The difference between day/night heart rate and blood pressure was considered a useful parameter of the influence of the circadian rhythm (Table 4).

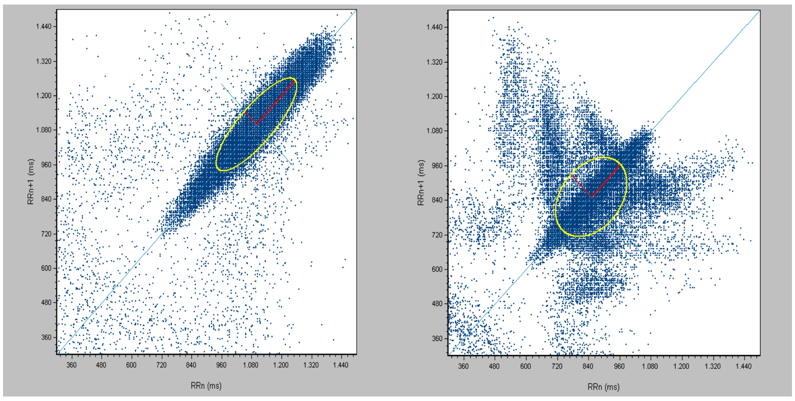
Table 4 The influence of arrhythmic events and heart failure in the hypertensive group

	Hypertension + events	Hypertension - events	P
N	**18**	29	
Age (yrs)	**60.5**	49.7	0.05
Mean heart rate (b/min)	**85**	84	Ns
LVEF (%)	**48**	68	0.005
SBP (mmHg)	**163**	160	Ns
DBP (mmHg)	**97**	107	Ns
Δ HR (b/min)	**9.65**	15.62	0.005
ΔSBP (mmHg)	**27.8**	23.72	0.05

During the study we did not observed significant differences between the absolute values of the systolic blood pressure inside the hypertensive group. Despite this fact some parameters like the difference between day and night mean heart rate could suggest important modulations of the tone autonomic tone in hypertension. More of this, ΔHR (b/min) and ΔSBP (mmHg), the later as expression of the day-night differences in systolic blood pressure, seemed to correlate. The role of the autonomic tone in essential hypertension was assessed using linear and nonlinear parameters. Heart rate variability and nonlinear dynamic parameters like entropy and detrended fractal analysis was applied to the ECG signals obtained from hypertensive patients. Even in a limited and selected group of patients it was difficult to identify vulnerable hypertensive patients. It seemed adequate to perform nonlinear analysis of the RR intervals in hypertensive patients to identify vulnerable patients.

5. Discussion

Heart failure remains nowadays one of the most important clinical condition. This observation is sustained by the high number of patients with heart failure worldwide. Despite numerous studies, the mortality in heart failure remains high. The incidence of ventricular arrhythmias, mainly ventricular tachycardia or ventricular fibrillation represents the most important conditions for sudden cardiac death. Comparing to control group or to patients without heart failure, like in hypertension, our study group was characterized by a high sympathetic tone, expressed by a high heart rate, high LF/HF ratio and altered nonlinear dynamic parameters (figure 2).



a b

Fig. 2 Nonlinear Dynamic Analysis in control group (a) and heart failure group (b)

We noticed an important association between variability and complexity organization of heart beat fluctuations that might be specific for the process of autonomic imbalance in heart failure and suggests that there are alterations in the cardiac control mechanism associated with ischaemic heart failure.

The aim of the study was to offer significant data about the complex mechanisms involved in heart failure and hypertension. The most important aspect of this study is that even in the presence of early stages of heart diseases the autonomic tone mechanisms are involved in the outcome and prognosis and are detectable by noninvasive methods.

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