Experimental & Clinical Cardiology

Fractal scaling exponents of heart rate variability association with linear indices and Poincaré Plot

Original Article

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Abstract

The literature indicated that the fractal analysis of heart rate variability (HRV) is related to the chaos theory. However, it is not clear if the both short and long-term fractal scaling exponents of HRV are reliable for short period analysis in women. We evaluated the association of the fractal exponents of HRV with the time and frequency domain and geometric indices of HRV. We evaluated 65 healthy women between 18 and 30 years old. HRV was analyzed with a minimal number of 256 RR intervals in the time (SDNN, RMSSD, NN50 and pNN50) and frequency (LF, HF and LF/HF ratio) domains, the geometric index were also analyzed (triangular index-RRtri, triangular interpolation of RR intervals-TINN and Poincaré plot-SD1, SD2 and SD1/SD2) as well as short and long-term fractal exponents (alpha-1 and alpha-2) of the detrended fluctuation analysis (DFA). No significant correlation was observed for alpha-2 exponent with all indices. There was significant correlation of the alpha-1 exponent with RMSSD, pNN50, SDNN/RMSSD, LF (nu), HF (nu and ms^2), LF/HF ratio, SD1 and SD1/SD2 ratio. Our data does not indicate the alpha-2 exponent to be used for 256 RR intervals and we support the alpha-1 exponent to be used for HRV analysis in this condition.

Keywords: Autonomic nervous system; Cardiovascular system; Nonlinear dynamics; Physiology.

1. Introduction

The use of heart rate variability (HRV) as a method to investigate cardiac autonomic regulation has increased over the last decades. This term is well accepted in the literature as a method that evaluates the oscillations in the intervals between consecutive heartbeats (RR intervals), providing analysis of the influence of the sympathetic and parasympathetic nervous system on the heart [1].

For the HRV analysis, indexes obtained by linear methods, time and frequency domain, and nonlinear methods can be used. The linear methods of HRV analysis include time and frequency domain. The nonlinear methods is indicated to be predominant in human systems, due to its dynamic complex nature. It can not be evaluated accurately by the linear indices of HRV. In this sense, the chaos theory describes elements manifesting behaviors that are very sensitive to early situations, and they are difficult to repeat, however, they are deterministic elements [2].

Among the nonlinear indices of HRV use it may be included detrended fluctuation analysis (DFA). This method measures the presence or the absence of fractal correlation properties of the RR intervals [3]. The fractal analysis of HRV includes the short-term fractal exponent (alpha-1), that corresponds to a period of 4 to 11 beats, the long-term fractal exponent (alpha-2) that represents periods longer than 11 beats and the alpha-1/alpha-2 ratio. Alterations in fractal correlation properties of long- and short-term dynamics of HRV contribute to clinical professionals to prevent disorder development and also to identify autonomic injuries [4].

The DFA requests analysis above shorter intervals than the normally used 5–20 min. There are many indices that have proven useful in longer 5–20 min HRV analysis [2, 5]. However, it is not clear whether the alpha-2 exponent is useful for a minimum of 256 RR intervals. Therefore, in order to provide methodological data regarding those exponents, this study was undertaken to evaluate the association of the fractal exponents of HRV with the time and frequency domain and geometric indices of HRV for short period (minimal number of 256 RR intervals) in women.

3. Tables

4. Method

4.1 Study Population

We analyzed 65 healthy women aged between 18 and 25 years old, selected from our Institution. All volunteers were informed about the procedures and objectives of the study and, after agreeing, have signed a term of informed consent. All study procedures were approved by the Ethics Committee in Research of the Faculty of Sciences of the Univeridade Estadual Paulista, Campus of Marilia (Case No. CEP-2011-382) and followed the resolution 196/96 Council National Health 10/10/1996.

4.2 Non-inclusion criteria

We did not include subjects under the following conditions: body mass index (BMI) >35 kg/m^2; systolic blood pressure (SBP) >140 mmHg or diastolic blood pressure (DBP) >90 mmHg (at rest); cardiac arrhythmias (atrial flutter or fibrillation, multiple ventricular or atrial ectopy, second or third degree atrioventricular block), smoking, left ventricular dysfunction, neurological or respiratory

disorders and serious postural deviation in the chest such as severe scoliosis, kyphosis or hyperlordosis that could influence the respiratory pattern and treatment with drugs that influence cardiac autonomic regulation, i.e. beta adrenergic, beta-blockers, angiotensin agonists and antagonists.

4.3 Initial Evaluation

Before the experimental procedure, volunteers were identified by collecting the following information: age, gender, weight, height and body mass index (BMI). Weight was determined by using a digital scale (W 200/5, Welmy, Brasil) with a precision of 0.1kg. Height was determined by using a stadiometer (ES 2020, Sanny, Brasil) with a precision of 0.1 cm and 2.20 m of extension. Body mass index (BMI) was calculated using the following formula: weight (kg)/height (m²). We also measured systolic and diastolic blood pressure and heart rate.

4.4 Experimental protocol

Data were collected in our laboratory under controlled temperature (21° C–25° C) and humidity (50%–60%), and volunteers were instructed to avoid consuming alcohol, caffeine and substances that influence the autonomic nervous system for 24 hours before evaluation. Data were collected between 6 p.m. and 9 pm. All procedures necessary for the data collection were explained to the individuals, and the subjects were instructed to remain at rest and to avoid talking during the data collection.

After the initial evaluation the heart monitor strap was placed on each subject's thorax over the distal third of the sternum. The HR receiver (Polar RS800CX monitor, Polar Electro OY, Kempele, Finland) was placed on the wrist. The subject remained 10 minutes seated at rest with spontaneous breathing.

4.5 HRV analysis

The R-R intervals recorded by the portable HR monitor (with a sampling rate of 1000 Hz) were downloaded to the Polar Precision Performance program (v. 3.0, Polar Electro, Finland). The software enabled the visualization of HR and the extraction of a cardiac period (R-R interval) file in "txt" format. Following digital filtering complemented with manual filtering for the elimination of premature ectopic beats and artifacts, at least 256 R–R intervals were used for the data analysis. Only series with more than 95%

sinus rhythm was included in the study [6]. For calculation of the indices we used the HRV Analysis software (Kubios HRV v.1.1 for Windows, Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland) [7].

4.6 Time and frequency domain indices of HRV

To analyze HRV in the frequency domain, the low frequency (LF =0.04 to 0.15 Hz) and high frequency (HF = 0.15 to 0.40 Hz) spectral components were used in ms² and normalized units (nu), which represents a value relative to each spectral component in relation to the total power minus the very low frequency (VLF) components, and the ratio between these components (LF/HF). The spectral analysis was calculated using the Fast Fourier Transform algorithm [8].

The analysis in time domain was performed by means of SDNN (standard deviation of normal-to-normal R-R intervals), the percentage of adjacent RR intervals with a difference of duratio greater than 50ms (pNN50) and RMSSD (root-mean square of differences between adjacent normal RR intervals in a time interval) [9].

4.7 Geometric indices of HRV

The HRV analysis was performed using the following geometrical methods: RRtri, TINN and Poincaré plot (SD1, SD2 and SD1/SD2 ratio). The RRtri was calculated from the construction of a density histogram of RR intervals, which contains the horizontal axis of all possible RR intervals measured on a discrete scale with 7.8125 ms boxes (1/128 seconds) and on the vertical axis, the frequency with which each occurred. The union of points of the histogram columns forms a triangle-like shape. The RRtri was obtained by dividing the number of RR intervals used to construct the histogram by their modal frequency (i.e., the RR interval that most frequently appeared on RR).

The TINN consists of the measure of the base of a triangle. The method of least squares is used to determine the triangle. The RRtri and the TINN express the overall variability of the RR intervals.

The Poincaré plot is a map of points in Cartesian coordinates that is constructed from the values of the RR intervals. Each point is represented on the x-axis by the previous normal RR interval and on the y-axis by the following RR interval [11].

For the quantitative analysis of the plot, an ellipse was fitted to the points of the chart, with the

center determined by the average RR interval. The SD1 indices were calculated to measure the standard deviation of the distances of the points from the diagonal y=x, and SD2 measures the standard deviation of the distances of points from the line y=-x+RRm, where RRm is the average RR interval. The SD1 is an index of the instantaneous recording of the variability of beat-to-beat and represents the parasympathetic activity, whereas the SD2 index represents the long-term HRV and reflects the overall variability. The SD1/SD2 shows the ratio between the short- and long-term variation among the RR intervals.

The plot was qualitatively analyzed using HRV analysis software based on the figures formed by its attractor. The expected shapes were described by Tulppo et al. as [4]:

1) Figures in which an increase in the dispersion of RR intervals is observed with increased intervals, characteristic of a normal plot.

2) Small figures with beat-to-beat global dispersion without increased long-term dispersion of RR intervals.

4.8 Fractal analysis of HRV

For the analysis of the fractal properties of the heart rate, detrended fluctuation analysis (DFA) was applied to a time series of the R–R intervals obtained from the participants. The procedure for the calculation of DFA is made up of the following steps:

The R–R series obtained experimentally is integrated using the expression:

$$Y(k) = \sum_{i=1}^{k} [RR(i) - RR_{ave}]$$

in which Y(k) is the k-th term of the integrated series (k = 1, 2,..., N); R–R(i) is the i-th value of the R–R intervals; and R–R$_{ave}$ is the mean of the R–R intervals of the original series, with N length:

$$RRave = \frac{1}{N}\sum_{i=1}^{N} RR(i)$$

The integrated time series is then divided into intervals with a length of n, (n = 1, 2,..., N). In each of these intervals, the local trend of the series is calculated by a straight line of minimum squares adjusted to the data. The y-coordinate of this straight line was denominated Yn(k). The integrated series was then detrended [Y(k)], subtracting the local tendency Yn(k) in each interval. For a given interval of

size n, the size characteristic of the fluctuation for the integrated and detrended series is calculated by:

$$F(n) = \sqrt{\frac{1}{N}\sum_{K=1}^{N}[Y(k) - Yn(k)]^2}$$

This procedure is repeated for all intervals of size n, thereby obtaining a relation between the mean of the fluctuations [$F(n)$] and the size of the intervals (n). A linear relation on a log–log graph indicates a scale exponent law, based on the following formula:

$$F(n) \approx n\alpha$$

in which α is the scale exponent, which can be calculated by linear regression on a log–log graph (16). The following were calculated: short-term fractal exponent (alpha-1), corresponding to a period of 4 to 11 beats; long-term fractal exponent (alpha-2), corresponding to periods longer than 11 beats; and the alpha-1/alpha-2 ratio [12].

4.9 Statistical Analysis

Normal Gaussian distribution of the data was verified by the Shapiro-Wilk goodness-of-fit test (z value >1.0). For parametric distributions we applied the Pearson correlation test. For non-parametric distributions we used the Spearman correlation test. We performed correlation of the alpha-1 and alpha-2 exponents with the time and frequency domain and geometric indices of HRV. We considered weak correlation for r < 0.3, moderate correlation for r between 0.31 and 0.49 and strong correlation for r>0.5. Differences were considered significant when the probability of a Type I error was less than 5% (p < 0.05). We used the Software Biostat version 5.8.4 for Windows.

5. Results

Based on Table 1 we present the values regarding basal diastolic (DAP) and systolic arterial pressure (SAP), heart rate (HR), mean RR, weight, height and body mass index (BMI) of the volunteers.

We observe that the alpha-1 exponent was positive strongly and significantly correlated with mean HR, SDNN/RMSSD ratio, LF (nu) and LF/HF ratio. Moreover, there was negative correlation of the alpha-1 exponent with the RR intervals, RMSSD, pNN50, HF (ms²), HF (nu), SD1 and SD1/SD2 ratio (Table 2).

According to Table 3 we noted that the alpha-2 exponent of the DFA presented only moderate negative correlation with the LF index in absolute

units (ms²) with no significant correlation with any index.

In this context, we also evaluated the correlation of the alpha-1/alpha-2 ratio with the HRV indices and we observed positive correlation with mean HR, SDNN/RMSD ratio, LF (nu) and LF/HF ratio. Negative correlation of alpha-1/alpha-2 ratio was observed with mean RR interval, RMSSD, pNN50, HF (ms²), HF (nu), SD1 and SD1/SD2 ratio (Table 4).

6. Discussion

The DFA method is a revised root-mean-square analysis of a casual walk, and it measures the absence or presence of fractal correlation properties in the time series. In this method, a fractal-like signal results in an exponent value of ;1.0, a random signal results in a value of 0.5, and a strongly correlated signal behavior linear results in an exponent value of 1.5 [13]. In this study we investigated the association of the short and long-term fractal scaling exponents of HRV with the time and frequency domain and geometric indices of HRV in healthy women for a short period (minimal number of 256 RR intervals). We reported that the alpha-2 exponent was not associated with any index evaluated. Nevertheless, the alpha-1 exponent was strongly associated with those indices, whereas the alpha-1/alpha-2 ratio was partially associated.

Based on our data, the alpha-1 index analyzed in a minimal number of 256 RR intervals was positively correlated with mean HR, SDNN/RMSSD ratio, LF in normalized units and LF/HF ratio. LF/HF ratio corresponds to the sympathetic-vagal balance [1] while the LF is influenced by sympathetic and parasympathetic components of the ANS with a predominance of the sympathetic nervous system, but in normalized units it is more influenced by the sympathetic modulation [2]. Furthermore, the SDNN/RMSSD ratio is strongly indicated to present similar interpretation of the LF/HF ratio [14]. A very elegant study found that the decrease of the short-term fractal scaling exponent alpha-1 revealed the loss of the short-term fractal correlation properties of HR dynamics toward more random HR dynamics during a stress condition, i.e. cold face immersion. Indeed, the indices that were associated with the alpha-1 in our study (LF and LF/HF ratio) are used to be influenced by this test [4]. Similar to our data, sympathoexcitation via infusion of norepinephrine was showed to decrease the alpha-1 exponent in a dose-responsive manner [15], while sympathetic

blockade presents smaller effects on fractal HR dynamics [16]. The mentioned study in animals and our finding indicate that the alpha-1 exponent presents a positive association with the sympathetic-vagal balance of cardiac modulation.

We also observed that the short-term fractal scaling exponent alpha-1 presented negative correlation with mean RR interval, RMSSD, pNN50, HF in absolute (ms²) and normalized units (nu), SD1 and SD1/SD2 ratio. It supports the inverse proportion of alpha-1 exponent with the HRV indices that represents the parasympathetic modulation of the heart, i.e. RMSSD and pNN50 time and HF frequency domain indices. Also, vagal blockade with high dose atropine or glycopyrrolate was observed to increase the short-term scaling alpha-1 exponent, while vagal stimulation with low dose atropine presented no significant effects on this exponent.

As expected, the alpha-1 exponent was indicated to be used for HRV analysis with a minimal number of 256 RR intervals. Although the alpha-1 exponent did not present significant correlation with the linear geometric indices (RRTri and TINN), it was strongly correlated with the non-linear Poincaré plot indices, i.e. SD1, SD2 and SD1/SD2 ratio. The Poincaré plot analysis is a tool that was firstly considered a qualitative tool and thereafter, it was used as a geometrical analysis, since it fits an ellipse to the shape of the Poincaré plot in order to calculate HRV indices [17]. This method is considered nonlinear, because it describes the nonlinear dynamics of a phenomenon that is able to identify the hidden correlation patterns of a time series signal [18]. Taken together, our data supports the term short-fractal scaling alpha-1 exponent as a non-linear index to evaluate HRV [2].

We revealed that alpha-1 exponent presented correlation with time and frequency domain indices of HRV. Physical exercise protocol was shown to improve time and frequency domain HRV indices [19]. Heffernan and coworkers [20] showed that exercise training improved fractal scaling properties of HRV in young men, irrespective of starting point (< 1 or >1). If suggestive of low fractal dynamics and less favorable cardiac health, whether HR dynamics approached white noise or Brownian noise at baseline HR fluctuations converged on pink noise after endurance exercise training. The authors also reported that this positive cardiac adaptation due to physical exercise training occurred despite no change in conventional risk factors such as fasting glucose, blood lipids, body fat of cardiorespiratory fitness.

In relation to the alpha-2 exponent, we found no significant correlation with any of the time and frequency domain and geometric indices of HRV. Although we did not report significant association of the long-term scaling alpha-2 exponent with the time and frequency domain and geometric indices of HRV, this exponent was indicated to represent Brownian motion. It is believed to represents collapse of the processes that regulate heart rate during pain and the total loss of the response loops, leading to highly correlated fractal dynamics that extent to many time scales [4]. This hypothesis supports the recent study published by the Weissman group [21], which reported significant increase in the alpha-2 during pain induction in newborns.

Similar to our results, previous studies did not find changes in alpha-2 exponent in different pathologic conditions [22, 11]. Carvalho and colleagues investigated the alpha-1 and alpha-2 exponents and time (SDNN, RMSSD and pNN50) and frequency (LF, HF and LF/HF ratio) domain indices of HRV in subjects with COPD and found reduced values of all time and frequency domain indices and decreased short-term fractal exponent, while there was no change in the alpha-2 exponent [11]. Vanderlei and coworkers [22] evaluated heart rate dynamics through analysis of the alpha-1 and alpha-2 fractal exponents and HRV frequency domain indices in obese children. The authors observed ecreased values of alpha-1 exponent, LF and HF indices in normalized units, however, they found no change was observed in the alpha-2 exponent. Additionally, it was previously suggested that the scaling exponent alpha-1 analysis may be useful for identifying high-risk patients while the alpha-2 exponent was not significantly associated with high-risk patients [23]. Nonetheless, a previous research observed a significant decrease in the short-term scaling exponent alpha-1 and a significant increase in the long-term scaling exponent alpha-2 during heel lancing in newborns [21]. We believe that the lack of physiological maturity in newborns may be involved in this response.

In our study we investigated only women between 18 and 25 years old in order to avoid gender and age-dependent effects. Previous investigations observed gender-related differences in relation to the sympathetic and parasympathetic modulation of the heart [24, 25]. It was observed that women present significantly increased global complexity of heart rate dynamics and greater high frequency compared to men [26]. In this sense, it was also reported that sex-based differences in psychophysiological responses are strongly influenced by hormonal status [27]. Furthermore, gender and age effects on nonlinear HRV indices reduce with increasing age [29].

Our study presents important data, indicating that the alpha-2 exponent of the DFA is not well associate with the other indices for a short term analysis (minimal number of 256 RR intervals). Nonlinear HRV indices provide information with respect to the complex structure and dynamics of interbeat time series. Nonlinear HRV indices provide a possibility to quantify "irregularity" of time series, which the usual time and frequency domain indices are not able to provide [2].

6. Conclusion

The short-term scaling alpha-1 exponent derived from DFA presented strong correlation with frequency and time domain and geometric indices of HRV whereas the alpha-2 exponent of the HRV was not associated those indices. Our results do not indicate the alpha-2 exponent to be used for 256 RR interval analysis of HRV in women at healthy condition.

7. Acknowledgements

8. References

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Table 1. Baseline diastolic (DAP) and systolic arterial pressure (SAP), heart rate (HR), mean RR interval, weight, height and body mass index (BMI) of the volunteers. Mean+standard-deviation. m: meters; kg: kilograms; bpm: beats per minut; mmHg: millimeters of mercury.

Variable	Women
Age (years)	20.3±1.9
Height (m)	1.64 ±0.06
Weight (kg)	58.68 ±9.48
BMI (kg/m^2)	21.95 ±3.69
HR (bpm)	83.40 ±13.09
Mean RR (ms)	742 ±131.3
SAP (mmHg)	109.37 ±7.87
DAP (mmHg)	69.31 ±2.49

Table 2. Correlation between the alpha-1 exponent and the HRV indices. Mean RR: Mean RR intervals; Mean HR: mean heart rate; SDNN: standard deviation of normal-to-normal R-R intervals; pNN50: the percentage of adjacent RR intervals with a difference of duration greater than 50ms; RMSSD: root-mean square of differences between adjacent normal RR intervals in a time interval. ms: millisecond. LF: low frequency; HF: high frequency; LF/HF: low frequency/high frequency ratio; RRtri – Triangular index; TINN – triangular interpolation of RR intervals; SD1 – standard deviation of the instantaneous variability of the beat-to beat heart rate; SD2 – standard deviation of long-term continuous RR interval variability; SD1/SD2 ratio – ratio between the short - and long - term variations of RR intervals. ms: milliseconds; nu: normalized units.

Index	r	p
Mean RR	-0.57	p<0.0001
Mean HR	0.57	p<0.0001
SDNN	-0.23	0.07
RMSSD	-0.57	p<0.0001
SDNN/RMSSD	0.68	p<0.0001
pNN50	-0.61	p<0.0001
RRtri	-0.19	0.12
TINN	-0.07	0.58
LF(ms²)	0.1	0.42
LF(nu)	0.77	p<0.0001
HF(ms²)	-0.61	p<0.0001
HF(nu)	-0.8	p<0.0001
LF/HF	0.8	p<0.0001
SD1	-0.62	p<0.0001
SD2	-0.09	0.49
SD1/SD2	-0.74	p<0.0001

Table 3. Correlation between the alpha-2 exponent and the HRV indices. Mean RR: Mean RR intervals; Mean HR: mean heart rate; SDNN: standard deviation of normal-to-normal R-R intervals; pNN50: the percentage of adjacent RR intervals with a difference of duration greater than 50ms; RMSSD: root-mean square of differences between adjacent normal RR intervals in a time interval. ms: millisecond. LF: low frequency; HF: high frequency; LF/HF: low frequency/high frequency ratio; RRtri – Triangular index; TINN – triangular interpolation of RR intervals; SD1 – standard deviation of the instantaneous variability of the beat-to beat heart rate; SD2 – standard deviation of long-term continuous RR interval variability; SD1/SD2 ratio – ratio between the short - and long - term variations of RR intervals. ms: milliseconds; nu: normalized units.

Index	r	p
Mean RR	0.16	0.21
Mean HR	-0.15	0.22
SDNN	0.03	0.82
RMSSD	0.01	0.92
SDNN/RMSSD	-0.01	0.93
pNN50	-0.01	0.96
RRtri	-0.06	0.65
TINN	0.04	0.76
LF(ms²)	-0.18	0.15
LF(nu)	0.04	0.76
HF(ms²)	-0.17	0.18
HF(nu)	-0.02	0.85
LF/HF	0.02	0.86
SD1	-0.01	0.97
SD2	0.04	0.74
SD1/SD2	-0.02	0.9

Table 4. Correlation between the alpha-1/alpha-2 ratio and the HRV indices. Mean RR: Mean RR intervals; Mean HR: mean heart rate; SDNN: standard deviation of normal-to-normal R-R intervals; pNN50: the percentage of adjacent RR intervals with a difference of duration greater than 50ms; RMSSD: root-mean square of differences between adjacent normal RR intervals in a time interval. ms: millisecond. LF: low frequency; HF: high frequency; LF/HF: low frequency/high frequency ratio; RRtri – Triangular index; TINN – triangular interpolation of RR intervals; SD1 – standard deviation of the instantaneous variability of the beat-to beat heart rate; SD2 – standard deviation of long-term continuous RR interval variability; SD1/SD2 ratio – ratio between the short - and long - term variations of RR intervals. ms: milliseconds; nu: normalized units.

Index	r	p
Mean RR	-0.5	$p < 0.0001$
Mean HR	0.5	$p < 0.0001$
SDNN	-0.17	0.17
RMSSD	-0.52	$p < 0.0001$
SDNN/RMSSD	0.66	$p < 0.0001$
pNN50	-0.55	$p < 0.0001$
RRtri	-0.13	0.31
TINN	-0.07	0.58
LF(ms²)	0.16	0.2
LF(nu)	0.75	$p < 0.0001$
HF(ms²)	-0.51	$p < 0.0001$
HF(nu)	-0.76	$p < 0.0001$
LF/HF	0.76	$p < 0.0001$
SD1	-0.55	$p < 0.0001$
SD2	-0.05	0.67
SD1/SD2	-0.69	$p < 0.0001$