

Non-Linear Dynamics in Patients with Stable Angina Pectoris

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Abstract

Dynamic analysis techniques may quantify abnormalities in heart rate behaviour based on non-linear and fractal analysis. To investigate the clinical and prognostic significance of fractal dimension and detrended fluctuation analysis, the group of patients with stable angina pectoris without previous myocardial infarction, and age-matched healthy control were studied. The fractal dimension of the R-R series was determined by the range rescaled analysis technique. To quantify fractal long-range-correlation properties of heart rate variability, the detrended fluctuation analysis technique was used. The short-term fractal scaling exponent (α_1) was significantly lower in patients with stable angina pectoris (0.95 ± 0.05 vs. 1.08 ± 0.06 ; $p < 0.05$). The patients with stable angina pectoris had higher fractal dimension than healthy control group ($P < 0.01$).

1. Introduction

Heart rate variability (HRV) reflects the modulation of cardiac function by autonomic and other physiological systems, and its measurements from electrocardiography (ECG) recordings during an exercise ECG test may be the useful method for both clinical and scientific purposes [1].

Traditional statistical measures provide limited information about HRV, because non-linear mechanisms may also be involved in the genesis of HR dynamics [2]. A number of new methods have been recently developed to quantify complex heart rate dynamics. They may uncover abnormalities in the time series data, which are not apparent using conventional linear statistic methods [3].

This study tested the hypothesis that fractal measurements of HRV are altered in patients with stable angina pectoris.

2. Methods

2.1. Patients

The twenty-five consecutive patients with stable angina pectoris and without previous myocardial infarction were included in the series, after history of chest pain and non-invasive cardiovascular diagnostic measurements (ECG at rest, echocardiography, 24-hours ECG, vectorcardiography, exercise ECG test and laboratory coronary risk factors data), with ECG evidence of ischemic ST-segment depression (≥ 0.1 mV) during an exercise test.

They were 57 ± 6 years old, 12 male. No cardiac medication was allowed on day of testing, and β -blocking therapy had been withdrawn at least 7 days before and calcium antagonists at least 2 days before.

Patients with silent ischemia during the 24-hour ECG recording and diabetes mellitus were excluded.

The control group consisted of 20 randomly selected age-matched (mean age 58 ± 8 years), and sex-matched (11 male) healthy subjects.

All controls after a complete non-invasive examination and their medical history revealed no cardiovascular disease or use of medication. They had normal ECG at rest, echocardiography data (M-mode, 2-D dimensional and Doppler echocardiography), 24-hours ECG recording, normal arterial blood pressure and fasting blood glucose.

An exercise ECG on all subjects was obtained using a symptom or ECG changes limited test. A horizontal or down sloping ST-segment depression of ≥ 0.1 mV occurring 0.08 second after the J point was considered to be of ischemic origin.

2.2. Analysis of HRV

Series of R–R intervals were obtained from high resolution ECG during the exercise ECG test (sampling frequency 1000 Hz), and the recording time scale was approximately about 1500 beats. The ECG data were digitised by the WaveBook 512 (Iotech. Cal. USA), and transferred to a computer for analysis.

The R–R interval series was passed through a filter that eliminates noise, artefacts and premature beats. All R–R interval series was first edited automatically, after which careful manual editing was performed by visual inspection of the each R–R interval. After this, all questionable portions were excluded manually, and only segments with > 85 % sinus beats were included in final analysis.

The fractal dimension of the R–R interval series was determined by the «range rescaled analysis» (R/S): $\{R(n) / S(n) \sim n^H\}$, where H is the Hurst's exponent (H). Hurst's exponent (H) = $\log(R / S) / \log(n)$ where n is the length of the time box.

Hurst's exponent approximately about 0.5 represents ordinary random walk or Brownian motion. If the H is < 0.5, it means negative correlation between the increments or ant persistent time series, and if H is > 0.5, it represents positive correlation between the increments or persistent natural series.

Hurst's exponent is related to the fractal dimension (FD): $H = E + 1 - FD$, where E is the Euclidean dimension (E = 0 for point, 1 for line and 2 for surface). Relation between H and FD of the graph of a random fractal is: $FD = 2 - H$ for one-dimensional signal. While H vary from 0 – 1, FD decreasing from 2 to 1.

Hurst's exponent as well as fractal dimension was determined separately for each program of exercise test including 30 seconds baseline ECG before the exercise and six minutes of relaxation after the exercise test.

To quantify fractal long-range correlation properties of the HRV, the detrended fluctuation analysis (DFA) technique, which is a modified root–mean–square analysis of a random walk, was used.

The method quantifies the presence or absence of fractal long–range correlation properties. The root–mean–square fluctuation of integrated and detrended time series is calculated by formula:

$$F(n) = \sqrt{1/N \sum_{k=1}^n [y(k) - y_n(k)]^2}$$

This calculation was repeated over all time scales (box size) to characterize the relationship between F(n), the average fluctuation, as a function of box size. Typically, F(n) will increase with box size n. A linear relationship on a log–log plot indicates the presence of power law (fractal) scaling.

In this study, HRV was characterized by a scaling exponent α , the slope of the linear relating $\log F(n)$ to $\log(n)$, separately for short term (≤ 11 beats, α_1), and long term (≥ 11 beats, α_2) fluctuations in the R–R series data (Figure 1).

Results are expressed as mean \pm standard deviation (SD). A p value < 0.05 was considered significant.

3. Results

The baseline clinical and heart rate variables of healthy controls and patients with stable angina pectoris are listed in Table 1. There were no differences observed in conventional statistical linear measures of HRV (average RR intervals and SDNN in time domain and LF/HF ratio in frequent domain). The fractal dimension calculated over Hurst's exponent was significantly higher in patients with stable angina pectoris. The results of exercise data set show existence of crossover phenomena between short time scales by the DFA method. It was found a significant difference between patients with stable angina pectoris and healthy controls in short time scales (0.95 ± 0.05 vs. 1.08 ± 0.06) (Figure 1). The healthy subjects typically show physiologic fractal behaviour of heartbeat dynamics, while the patients with SAP show an alteration in fractal correlation properties. There were no differences for the long-term series.

Clinical data (n=45)	Healthy Controls (n=20)	Patients with SAP (n= 25)
Age (yrs)	58 ± 8	57 ± 6
Men / women	11/9	12/13
ECG at rest (freq.)	74	81
VPCs / hour	3 ± 0.7	4 ± 2.7
LV ejection fraction (%)	71 ± 6	63 ± 9
E/A wave (m/s)	1.4 ± 0.2	0.8 ± 0.2
Exercise ECG data:		
Average RR interval (ms)	874 ± 108	856 ± 114
SDNN (ms)	149 ± 41	139 ± 40
LF/HF ratio	3.2 ± 1.5	3.5 ± 1.7
Hurst's exponent	0.96 ± 0.05	0.68 ± 0.07 *
Fractal dimension	1.04 ± 0.07	1.32 ± 0.09 +
α_1	1.08 ± 0.06	0.95 ± 0.05 *
α_2	1.39 ± 0.04	1.36 ± 0.26

Table 1. The clinical and heart rate variables of subjects in the study (* P value < 0.05; + P value < 0.01) [legend] ECG= electrocardiography; VPCs= ventricular premature contractions; LV= left ventricular; SDNN= standard deviation of all RR intervals; LF= low frequency; HF= high frequency; α = fractal-like scaling exponent from detrended fluctuation analysis.

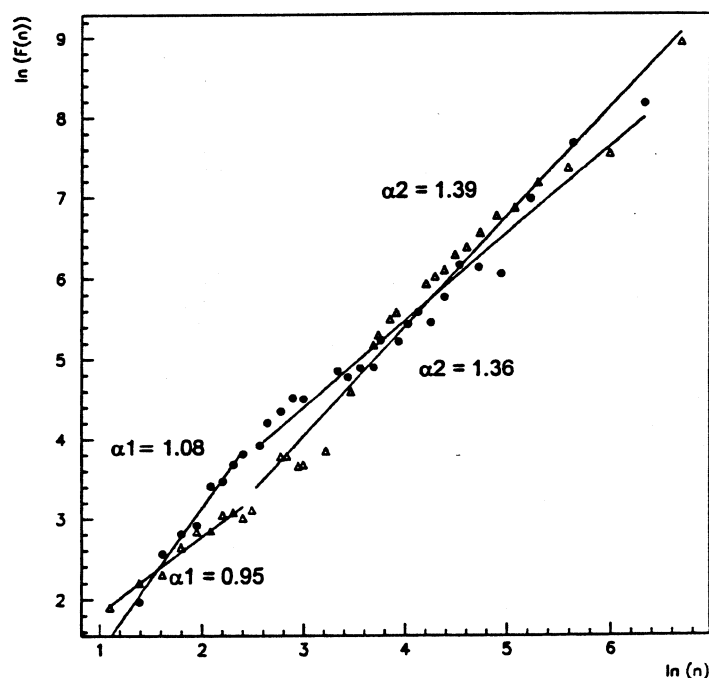


Figure 1. Examples of detrended fluctuation analysis data
 Δ patients with stable angina pectoris
 • healthy subjects

4. Conclusions

Results of this study do not allow conclusions regarding the lack of prognostic value of traditional measurements of HRV because of a relative small patient population, but does give preliminary information on the usefulness of fractal analysis methods in risk stratification of patients with stable CHD.

Patients with stable angina pectoris had loss normal fractal characteristics in heart rate variability estimated by non-linear dynamics evaluation of heart rate behaviour. The measurement of a short-term fractal-scaling exponent gives complementary information on abnormal HR behaviour in patients with SAP than that other measurement.

The present study shows that normal fractal properties of R-R interval dynamics is altered in patient with SAP estimated by R/S and DFA methods. Dynamic analysis of HRV gives independent information that possible cannot be detected by traditional linear analysis technique.

Healthy subjects have a distinct circadian rhythm of HRV, but this rhythm seems to be blunted in coronary heart disease (CHD) patients [4]. Fractal correlation properties and fractal dimension in this study may reflect altered neuroanatomic interaction that may predispose to the development of CHD.

Further studies in larger population will be needed to further define the clinical utility of new fractal measurements of HRV for risk stratification in patients with CHD.

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