Multifractal Properties of the Heart Rate Dynamics during Acute Myocardial Ischemia

R Magrans[1,2], P Gomis[1,2], P Caminal[1,2], G Wagner[3]

[1]Departament ESAII, Universitat Politècnica de Catalunya, Barcelona, Spain
[2]CIBER de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain
[3]Duke University Medical Center, Durham, North Carolina, USA

Abstract

The purpose of this study was to assess the dynamics of the heart rate during myocardial ischemia produced by long PTCA procedures using multifractal signal properties. We found significant complex reactions due to the effects of coronary occlusion on the autonomic control of the cardiac rhythm which suggests that the multifractal indices may be a promising non-linear technique to evaluate the autonomous nervous system response in presence of transient myocardial ischemia.

1.   Introduction

Myocardial ischemia is a consequence of coronary artery disease. The percutaneous transluminal coronary angioplasty (PTCA), used to improve circulation, has been a good model to evaluate myocardial ischemia.

It has been shown that cardiovascular diseases are related with alterations of the autonomic nervous system (ANS) provoking an imbalance between antagonistic activity of parasympathetic and sympathetic subsystems which it is traduced on a reduction in the multifractal properties of the R-R signal [1,2].

Experimental studies have demonstrated that coronary occlusion activates afferent cardiac sympathetic nerves, driving a sympathetic reflex [3]. On the other hand, Manfrini et al. [4] have been assessed the ANS activity during spontaneous and balloon-induced ischemia by heart rate variability (HRV) analysis in frequency domain showing that balloon inflation and occlusion evoke a parasympathetic predominance, whereas spontaneous occlusion produce a sympathetic activation. Other studies have also evaluated the symphato-vagal activity behaviour during prolonged PTCA on different coronary arteries using time-frequency representations [5], and non-linear methods [6-8].

The aim of this study is to quantify the dynamics of the autonomic control of the cardiac rhythm during ischemic events provoked by long PTCA procedures through indices extracted from multifractal analysis.

2.   Materials and methods

2.1.   Database and study protocol

The study was based on patients from the STAFF3 database undergoing elective PTCA in the catheterization laboratory at Charleston Area Medical Center, West Virginian, USA [9].

Fifty five patients who met the following criteria were considered in the study: (a) no history of coronary bypass surgery, without left or right ventricular hypertrophy; (b) no evidence of right bundle branch block; (c) QRS duration less than 120 ms measured on a previous control ECG; (d) no clinical or ECG evidence of previous myocardial infarction; and (e) artery occlusion duration of at least 3 minutes.

Patients were classified according to the occluded coronary artery in three groups: right coronary artery (RCA) with 25 patients, left anterior descending (LAD) coronary artery with 20 patients, and left circumflex coronary artery (LCX) with 10 patients. Depending on the position of the balloon with respect to the aorta the patients were also classified in other three groups: proximal (PROX) occlusion (31 patients; among them 10 were classified in RCA, 13 in LAD, and 8 in LCX); mid (MID) occlusion (13 patients; 8 in RCA, 4 in LAD, and 1 in LCX); distal (DIST) occlusion (7 patients; 6 in RCA, and 1 in LCX). Four patients could not be included in the last classification because the occlusions were located in other positions.

The analysis were performed using 3 minutes of R-R signal from the pre-inflation ECG (pre-PTCA), the first 3 minutes (PTCA1) and the last 3 minutes (PTCA2) of the ECG during PTCA, and 3 minutes corresponding to reperfusion period (post-PTCA). Also, we analyzed two set of R-R control signals obtained from ECG registered 24 hours before (pre24) and after (post24) the PTCA procedure corresponding to 30 patients of the total used for the study. All series were resampled at 5 Hz in order to obtain uniformly sampled data.

2.2. Multifractal analysis

We used the multifractal detrended fluctuation analysis (MF-DFA) method [10] to perform a multifractal characterization of the signals.

The integrated R-R signal Y(i) was divided into non-overlapping windows v of equal length s. In each window a 2nd order polynomial P_v was fitted to Y(i) in the least-squares sense and the trend of the window was eliminated. Next, the variance $F^2(s,v)$ of the integrated and detrended signal for each window was calculated. The contribution of a certain window to fluctuations of a signal was determined by the fluctuation function $F_q(s)$ constructed as the qth root of the mean of the q/2-th powers of $F^2(s,v)$ over all windows of length s.

The multifractal spectrum $\tau(q)$ was obtained from $F_q(s)$ according to $F_q(s) \sim s^{1+\tau(q)}$ power-law and it was used to find the singularity spectrum $f(\alpha)$ via Legendre transform,

$$\alpha = \frac{d\tau(q)}{dq} \text{ and } f(\alpha) = q\alpha - \tau(q) \tag{1}$$

where α is the singularity exponent.

Finally, we used the width of $f(\alpha)$ defined as $\Delta\alpha = \alpha_{max} - \alpha_{min}$, where α_{min} and α_{max} are the minimum and maximum values of the set of singularity exponents respectively to detect the multifractality degree; whereas the value α_m of the singularity exponent when $f(\alpha)$ is maximum was used to measure the long-range dependence on the fluctuations of the heartbeat dynamics.

2.3. Statistical analysis

A Wilcoxon nonparametric rank-based test was used in order to assess the statistical significance when comparing values of the indices between different periods. Significant differences were taken into account when $p < 0.05$. All analyses were performed with the SPSS for Windows release 15.0 (SPSS Inc., Chicago, Ill).

3. Results

3.1. Derived from R-R signals during PTCA procedures

The multifractal indices revealed changes associated with ischemia provoked by coronary artery occlusions.

The averaged singularity spectra for the studied groups and for the entire set of patients obtained before inflation, during balloon inflation and after occlusion are represented on figures 1 and 2 respectively. In all cases, the width of $f(\alpha)$ increased considerably from pre-inflation to reperfusion and it was centred on a larger value of the singularity exponent for post-PTCA period. This situation is shown quantitatively on Table 1.
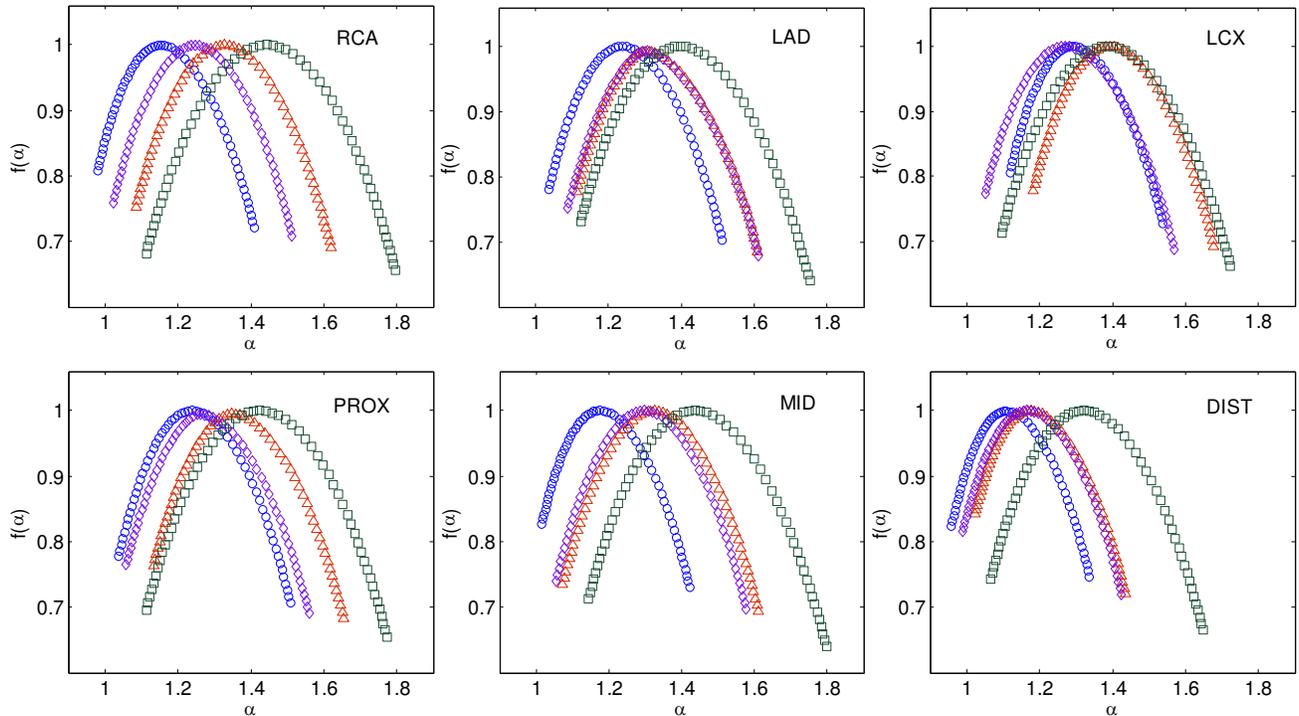

Figure 1. The averaged singularity spectra for the episodes: pre-PTCA (○), PTCA1 (Δ), PTCA2 (◊), and post-PTCA (□) in each group.

Table 1. Mean ± standard deviation values and p-value for Wilcoxon nonparametric rank-based test: p^*, pre-PTCA vs. PTCA1; p^{**}, pre-PTCA vs. PTCA2; p^+, pre-PTCA vs. post-PTCA; p^{++}, PTCA1 vs. PTCA2; $p^{\dagger}$, PTCA1 vs. post-PTCA; $p^{\ddagger}$, PTCA2 vs. post-PTCA

Group	Indices	Episode				p-value					
		pre-PTCA	PTCA1	PTCA2	post-PTCA	p^*	p^{**}	p^+	p^{++}	$p^{\dagger}$	$p^{\ddagger}$
RCA	$\Delta\alpha$	0.43 ± 0.15	0.53 ± 0.18	0.49 ± 0.17	0.68 ± 0.20	0.007	0.143	< 0.001	0.274	0.001	< 0.001
25 pts.	α_m	1.15 ± 0.13	1.33 ± 0.25	1.25 ± 0.18	1.44 ± 0.27	0.004	0.030	< 0.001	0.014	0.045	0.002
LAD	$\Delta\alpha$	0.48 ± 0.15	0.50 ± 0.15	0.53 ± 0.17	0.63 ± 0.17	0.538	0.313	0.028	0.356	0.028	0.135
20 pts.	α_m	1.24 ± 0.20	1.32 ± 0.23	1.32 ± 0.21	1.40 ± 0.14	0.076	0.126	0.006	0.943	0.167	0.086
LCX	$\Delta\alpha$	0.42 ± 0.11	0.49 ± 0.14	0.52 ± 0.19	0.63 ± 0.12	0.169	0.114	0.007	0.508	0.028	0.114
10 pts.	α_m	1.29 ± 0.16	1.39 ± 0.18	1.27 ± 0.19	1.39 ± 0.19	0.139	0.878	0.508	0.009	0.799	0.139
PROX	$\Delta\alpha$	0.47 ± 0.13	0.52 ± 0.16	0.50 ± 0.18	0.66 ± 0.15	0.098	0.399	< 0.001	0.894	< 0.001	0.001
31 pts.	α_m	1.24 ± 0.16	1.36 ± 0.20	1.27 ± 0.17	1.43 ± 0.21	0.005	0.389	0.001	0.001	0.142	0.003
MID	$\Delta\alpha$	0.41 ± 0.16	0.54 ± 0.16	0.52 ± 0.09	0.65 ± 0.19	0.039	0.033	0.005	0.657	0.152	0.019
13 pts.	α_m	1.18 ± 0.22	1.33 ± 0.18	1.30 ± 0.20	1.44 ± 0.19	0.033	0.133	0.006	0.534	0.064	0.087
DIST	$\Delta\alpha$	0.38 ± 0.18	0.41 ± 0.19	0.44 ± 0.16	0.58 ± 0.23	0.398	0.176	0.063	0.398	0.043	0.063
7 pts.	α_m	1.11 ± 0.12	1.18 ± 0.39	1.17 ± 0.21	1.32 ± 0.32	0.866	0.499	0.128	0.866	0.310	0.091
ALL	$\Delta\alpha$	0.44 ± 0.14	0.51 ± 0.16	0.51 ± 0.17	0.65 ± 0.18	0.005	0.024	< 0.001	0.958	< 0.001	< 0.001
55 pts.	α_m	1.21 ± 0.17	1.34 ± 0.23	1.28 ± 0.19	1.42 ± 0.22	< 0.001	0.021	< 0.001	0.002	0.021	< 0.001

According to the occluded coronary artery, RCA group showed bigger differences than LAD and LCX groups. In this group, α_m changed in a significant manner through all procedure; whereas for $\Delta\alpha$ index, significant differences were found too except when comparing PTCA2 vs. pre-PTCA and intra-PTCA values. For LAD group, both $\Delta\alpha$ and α_m indices increased significantly during post-PTCA compared to pre-PTCA ($\Delta\alpha$ was from 0.48 ± 0.15 to 0.63 ± 0.17, p = 0.028; α_m was from 1.24 ± 0.20 to 1.40 ± 0.14, p = 0.006); the value of the indices also augmented during PTCA periods respect to pre-inflation but without statistical relevance. When comparing reperfusion period with the period before balloon inflation only $\Delta\alpha$ index showed a significant change (p = 0.007) on LCX group.

Considering the position of the balloon occlusion with respect to the aorta, a significant increase was found in the value of the indices during reperfusion respect to pre-PTCA on PROX and MID groups. For PROX occlusions statistically significant differences were also found when comparing the indices values between post-PTCA and PTCA2 although with a lower significance than the former. Besides, significant changes were found in the value of some indices in other comparisons. For DIST occlusions only a significant change was observed in $\Delta\alpha$ index comparing post-PTCA with PTCA1 (from 0.41 ± 0.19 to 0.58 ± 0.23, p = 0.043).

For the entire set of occluded arteries, post inflation period showed a statistically significant increase (p < 0.001) in $\Delta\alpha$ compared to pre-inflation and during balloon occlusion. $\Delta\alpha$ also showed significant differences in PTCA values with respect to pre-PTCA (p = 0.005 and p = 0.024). The α_m index increased significantly in all periods compared, except in PTCA1 versus PTCA2, where it experimented a significant decrease (from 1.34 ± 0.23 to 1.28 ± 0.19, p = 0.002).
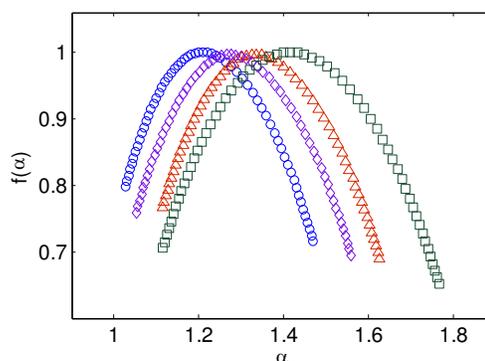

Figure 2. The averaged singularity spectra considering all patients during pre-PTCA (○), PTCA1 (△), PTCA2 (◇), and post-PTCA (□) episodes.

3.2 Derived from R-R control signals

Next, the averaged singularity spectra extracted from the R-R signals recorded 24 hours before and after the PTCA procedure are shown on Figure 3. The mean value and standard deviation of the indices in the pre24 and post24 periods, as well as the p-values in each comparison are show on Table 2.
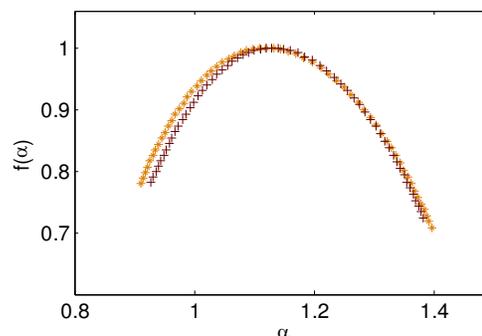

Figure 3. The averaged singularity spectra from R-R control signals for pre24 (*) and post24 (+) periods.

Table 2. Mean ± standard deviation of multifractal indices extracted from R-R control groups and p-value for Wilcoxon nonparametric rank-based test: p^*, pre24 vs. post24; p^{**}, pre-PTCA vs. pre24; p^+, PTCA1 vs. pre24; p^{++}, PTCA2 vs. pre24; p°, post-PTCA vs. pre24; $p^{\dagger}$, PTCA1 vs. post24; $p^{\ddagger}$, PTCA2 vs. post24; $p^{\bullet}$, post-PTCA vs. post24

p-value	pre24/post24	
	$\Delta\alpha$	α_m
	$0.49 \pm 0.20 / 0.46 \pm 0.16$	$1.14 \pm 0.18 / 1.13 \pm 0.21$
p^*	0.517	0.517
p^{**}	0.781	0.131
p^+	0.813	0.003
p^{++}	0.600	0.016
p°	0.002	< 0.001
$p^{\dagger}$	0.192	< 0.001
$p^{\ddagger}$	0.813	0.004
$p^{\bullet}$	< 0.001	< 0.001

No significance differences were observed in the value of the indices calculated 24 hours after PTCA procedure respect to the values calculated 24 hours before procedure. Comparing the indices values for pre-PTCA period with the values obtained in pre24 no significant differences were found neither. The indices showed significant changes in both pre24 and post24 periods versus post-PTCA period. Significant differences were also found in α_m index when comparing both pre24 and post24 to PTCA periods.

4.   Discussion and conclusions

The indices revealed significant augment during transient ischemia and reperfusion periods, indicating an increase in the multifractality of short-term R-R signal and a decrease of the long-range dependence on heartbeat fluctuations, which may represent a beneficial adaptive mechanism for increasing coronary flow.

The differences were more notable in patients with RCA-PROX occlusions, which may be related to different responses of the ANS according to the site of the ischemia.

Results derived from R-R control analysis show that the signals during pre-inflation were not affect by external factors associated with the preparation of the procedure in the catheterization laboratory, suggesting that the changes were uniquely consequence of coronary occlusion effects on the autonomic control of the cardiac rhythm. When PTCA has finished, the cardiovascular system seems recovering to the initial conditions after a certain period of time.

Our results are in correspondence with another study [8] over the Staff3 database which introduced an index to quantify the nonlinear content of the R-R signal combining surrogate data and average mutual information.

We think that the multifractal indices used here may be a promising non-linear technique to assess the dynamics of autonomic control of the heart in presence of ischemia.

References

[1] Ivanov PCh, et al. From 1/f noise to multifractal cascades in heartbeat dynamics. Chaos 2001; 11:641-52.

[2] Goldberger AL, et al. Fractal dynamics in physiology: Alterations with disease and aging. PNAS 2002; 99:2466-72.

[3] Malliani A, Schwartz JP, Zanchetti A. A sympathetic reflex elicited by experimental coronary occlusion. Am J Physiol 1969; 217:703-9.

[4] Manfrini O, Morgagni G, Pizzi C, Fontana F, Bugiardini R. Changes in autonomic nervous system activity: spontaneous versus balloon-induced myocardial ischaemia. European Heart Journal 2004; 25:1502-8.

[5] Clariá F, Vallverdú M, Caminal P. The effects of coronary occlusion location on RR signal. IEEE Eng Med Biol 2002; 21:59-64.

[6] Gomis P, Caminal P, Vallverdú M, Warren S, Wagner G. Non-linear dynamic analysis of the cardiac rhythm during transient myocardial ischemia. Biomed Tech 2006; 51:178–81.

[7] Valencia JF, Vallverdú M, Gomis P, Wagner G, Caminal P. Multiscale information analysis of the autonomous nervous system during myocardial ischemia. Computers in Cardiology 2007; 34:589-92.

[8] Benitez R, et al. Characterization of the nonlinear content of the heart rate dynamics during myocardial ischemia. Med Eng & Phys 2009; 31:660-7.

[9] Ringborn M, Pahlm O, Wagner G, Warren S, Peterson J. The absence of high-frequency QRS changes in the presence of standard electrocardiographic QRS changes of old myocardial infarction. Am. Heart J. 2001; 141:573-9.

[10] Kantelhardt JW, et al. Multifractal detrended fluctuation analysis of nonstationary time series. Physica A 2002; 316:87-114.

Address for correspondence

Rudys Magrans Nicieza
Dept. ESAII, UPC
c/ Pau Gargallo 5, Edifici U, 08028, Barcelona, Spain
E-mail address: rudys.magrans@upc.edu