Autonomic Nervous System Response during Coronary Occlusion Evaluated with Multiple Factor Analysis of Standard and Fractal Indexes

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Abstract

The purpose of this study was to characterize the autonomic nervous system changes during a prolonged percutaneous transluminal coronary angioplasty (PTCA) procedure. This study used the records of 61 procedures from the Staff-3 database. Four stages were considered: 2 min of the pre-inflation ECG period; the first 2 min and last 2 min of the ECG during occlusion and 2 min immediately after balloon deflation. Standard and Fractal Indexes parameters from HRV analysis were extracted for each stage. Results show that the most important variables for the construction of the first axis were rMSSD and HF. The construction of the second axis depends mainly on the LF/(LF+HF) and fractal scalar exponent alfa-1. Results show that sympathetic activity increases during and after PTCA, and parasympathetic activity and complexity of ANS decreases during PTCA and increases in post-PTCA.

1. Introduction

The autonomic control of the heart is maintained not only by the efferent nerves emerging from the brain stem and the spinal cord but also by a local circuit of neurons included in the intrathoracic extracardiac and intrinsic cardiac ganglia, comprised by afferent and efferent neurons. These local cardiac circuits of neurons forming the intrinsic cardiac nervous system include afferent neurons, local circuit neurons, as well as sympathetic and parasympathetic efferent postganglionic neurons. Myocardial ischemia induced by coronary artery occlusions during balloon angioplasty is linked with cardiac control system reactions which may lead to heart failure. Therefore, the cardiovascular reflexes may become responsible for changes in heart rate or HRV, and even malignant arrhythmias [1].

Some experimental studies state that coronary occlusion activates afferent cardiac sympathetic nerves provoking a reflex sympathetic response and can modify the activity generated by intrinsic cardiac neurons [2]. Several studies in clinical evaluation of HRV during myocardial ischemia due to coronary occlusion have been reported [3]. These studies use standard time and frequency domain methods to evaluate the influence of the balance between sympathetic and parasympathetic activity, yielding different conclusions. Also, the usage of nonlinear fractal indices, which evaluate the complexity of heart rate dynamics, has emerged as a promising tool to enhance the predictive value of HRV for assessing malignant arrhythmias and the risk of sudden death after myocardial infarction, using short-duration R-R signals [4], [5], [6]). The main drawback in these studies is that no clarification is provided as to whether standard time and frequency domain or fractal parameters affect only the reflex sympathetic response or if parasympathetic modulation response is influenced as well.

The purpose of this study is to provide a characterization of ANS changes as a response over four periods of a PTCA procedure using a Multiple Factorial Analysis (MFA) of the standard time and frequency domain methods as well as nonlinear fractal indices from the R-R signal. MFA allows to reduce the number of variables, and to detect structures in the relationships between groups of variables and between groups of subjects.

Section 2 presents materials and methods used in this study. Protocols, parameters and MFA are described succinctly. Section 3 presents the results, which are further discussed in section 4.

2. Methods

2.1. Study protocol

This study used the Staff-3 database which is conformed by ECG records before, during and after prolonged PTCA in individual arteries. From 108 subjects, 70 patients were chosen on the basis of the following criteria: no evidence of previous myocardial infarction, QRS duration < 120 ms and no history of coronary bypass surgery. The 70 occlusions lasted at least 2 minutes (4.5 +/- 1.2 min). Four stages were considered: 2 min of the pre-inflation ECG (pre-PTCA) period; the first (leading) 2 min and last (trailing) 2 min of the ECG during occlusion (PTCAl and PTCA2, respectively) and 2 min immediately after balloon deflation (post-PTCA). Paired post-PTCA measurements were considered in 61 cases where segments lasted at least 2 min. Patients were classified according to the location of the coronary artery occlusion: 22 patients presented with left anterior descending coronary artery occlusion (LAD group), 12 patients with left circumflex coronary artery occlusion (LCX group) and 27 patients with right coronary artery occlusion (RCA group).

R-R signals were obtained from the lead with highest signal-to-noise ratio, using noise-robust software for R-wave detection and QRS wave delineation [7]. To assure the detection of normal sinus beats, artifacts and ectopic beats were removed from the R-R signal using a 5-beat sliding window algorithm rejecting any beat with a difference exceeding by 15% or more, the mean value of the window.

2.2. Standard and fractal HRV analysis

In this study, standard frequency domain HRV indices were measured from the power spectral density of the processed R-R signal using parametric auto-regressive modeling with the Burg method. R-R signal processing included removing its mean value and regular-spacing resampling at 3 Hz after interpolating the signal with cubic splines. The LF and HF bands were defined respectively by [0.04-0.15 Hz] and [0.15-0.4 Hz] as proposed by current guidelines [8]. For each stage of the protocol, RR intervals were obtained, and six classical HRV parameters were determined: RR mean, SD, rMSSD, LF, HF and LF/(HF+LF).

One of the scaling exponents used in this work is the power-law index β, computed in the range of 0.003 to 0.1 Hz (-2.5 to -1 in log scale). The second fractal index used is based on detrended fluctuation analysis (DFA) of R-R signal. This technique permits the detection of self-similar fluctuations included in an apparently non-stationary time series as the R-R signal and provides short-term fractal correlation properties of heart rate dynamics (Iyegar, 1996). The fractal correlation properties were measured by the scalar exponent, α_1. This study includes two fractal-like indices (β,α_1)

2.3. Statistical analysis

Multiple Factor Analysis (MFA) deals with data in which a set of individuals is described by several sets of variables. The MFA can be represented in three spaces: subject's space, variable's space and the spaces of groups of variables [10], [11].

We denote X the whole matrix, I the set of individuals, K set of the variables (all together), J the set of sub-groups such that $K = \bigcup_j K_j$ and X_j is the sub-matrix associated with group *j*. More precisely, the symbols I , J , K denote the set and their ordinal at once.

The principle of the MFA is based on the Principal Components Analysis (PCA) of the whole table. This analysis makes possible to balance the role of the groups of variables and provides a representation of the individuals and variables which are interpreted according to usual rules of PCA.

In a summarized form, the MFA on a series of groups of quantitative nature consists in performing, i) A PCA on the partial table X_j with the objective of balancing the influence between the groups. ii) A PCA of all the juxtaposed groups where each one of them has been previously weighed by the inverse of the root of the first eigenvalue coming from the partial PCA.

Later, the coordinates of the variables of each group are calculated with respect to the factors and a global representation is obtained.

In our study the data arise in the following form: $\boldsymbol{I}$=61 patients, $\boldsymbol{J}$ = 4 stages (pre-ptca, ptca1, ptca2, post-ptca) $\boldsymbol{K}$= 8 variables.

Finally, the comparisons were carried out using the test of Wilcoxon signed rank (test of equality of medians). The significant threshold was fixed at $p<0.05$.

3. Results

The inertia explained by the first two axes was 54% of total inertia (35.22% for the first axis and 18.22% for the second axis).

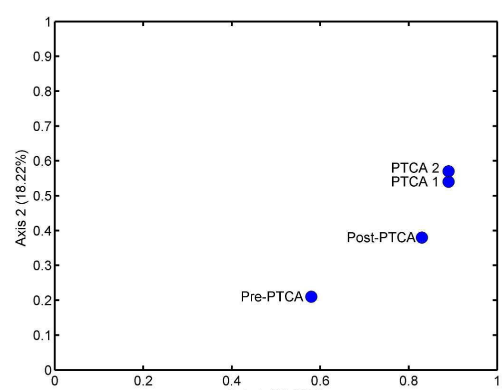

Figure 1. Four stages on first factorial plan.

The analysis of the contributions (see table 1) of the variables to each principal axis revealed the following: the most important variables for the construction of the first axis were rMSSD and HF. Also other variables contribute to this axis: SD and LF; considering that these parameters are associated to both parasympathetic and sympathetic modulation and that their contribution is less important, we can interpret this axis as a parasympathetic axis. The construction of the second axis depends mainly on the LF/(LF+HF) and fractal scalar exponent α_1. Axis 2 is interpreted as an axis of sympathetic drive response or ANS balance and is related to its degree of complexity.

Table 1. Variable's contributions to the principal axes.

	Contributions	
Pre-Ptca stage	Axis 1	Axis 2
HR_{pre}	2.9	0.8
SD_{pre}	2.8	0.2
$rMSSD_{pre}$	4.7	0.5
LF_{pre}	2.6	0.6
HF_{pre}	3.8	0.5
$LF/(LF+HF)_{pre}$	0.4	3.1
β_{pre}	0.0	0.3
α_{1pre}	1.0	6.5
Sub-total	18.2	12.6
Ptca1 stage	Axis 1	Axis 2
HR_{ptca1}	4.6	0.7
SD_{ptca1}	3.4	1.1
$rMSSD_{ptca1}$	6.4	1.3
LF_{ptca1}	5.1	3.0
HF_{ptca1}	6.6	0.7
$LF/(LF+HF)_{ptca1}$	0.3	11.0
β_{ptca1}	0.8	0.0
$\alpha_{1\ ptca1}$	0.6	13.7
Sub-total	27.8	31.6
Ptca2 stage	Axis 1	Axis 2
HR_{ptca2}	4.4	0.6
SD_{ptca2}	3.5	0.8
$rMSSD_{ptca2}$	6.5	1.3
LF_{ptca2}	5.1	3.4
HF_{ptca2}	7.1	0.8
$LF/(LF+HF)_{ptca2}$	0.2	13.6
β_{ptca2}	1.0	0.0
α_{1ptca2}	0.2	12.8
Sub-total	27.9	33.3
Post-Ptca stage	Axis 1	Axis 2
HR_{post}	3.4	1.2
SD_{ptca2}	3.5	1.8
$rMSSD_{post}$	5.7	0.1
LF_{post}	5.1	3.1
HF_{post}	7.2	0.0
$LF/(LF+HF)_{\ post}$	0.3	8.5
β_{post}	0.1	0.1
$\alpha_{1\ post}$	0.7	7.5
Sub-total	26.1	22.5

The first factor (parasympathetic axis) in Fig. 1 shows that parasympathetic drive decreases at PTCA (PTCA1 and PTCA2) and then tends to return to normal (post-PTCA). In the same way, the second factor shows that sympathetic response is increased during PTCA when compared to resting conditions; however during post-PTCA, sympathetic response continues to increase. This result could suggest that the ischemic condition is still present during post-PTCA period.

Figure 2 shows the averaged subjects (over the four stages) on first factorial plan. Among the LCX group patients, the second factor is more significant than in patients included in the other groups ($p<0.01$).

We have compared the most relevant parameters for each axe. For axis 1, figure 3 shows that rMSSD and HF index lessened significantly ($p<0.001$) during PTCA (PTCA1 and PTCA2) and after balloon deflation ($p<0.001$). Checking every group, we found that HF and rMSSD index decreased significantly in LAD and RCA groups ($p<0.001$). LCX occlusions did not produce any significant change on parasympathetic modulation. Also no differences in these indices were found between the leading and trailing periods.

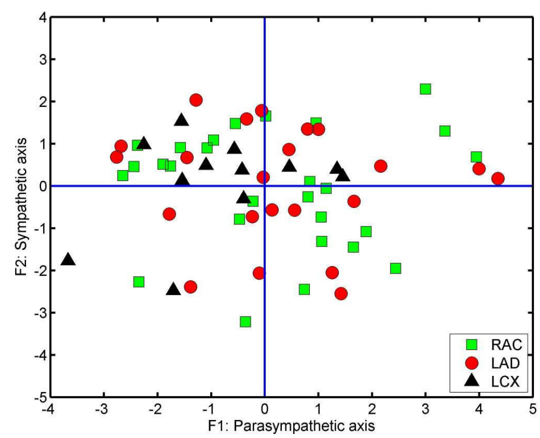

Figure 2. Averaged subjects on first factorial plan.

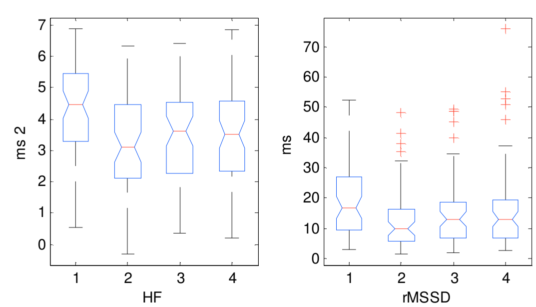

Figure 3. RMSSD and HF index evolution

For axis 2, figure 4 shows that values for LF/(LF+HF) and α_1 augmented significantly ($p<0.001$) after balloon deflation in relation to PTCA1 ($p<0.001$) , PTCA2 ($p<0.001$) and pre-PTCA($p<0.001$) measurements. In addition, these findings were not observed in the LCX group.

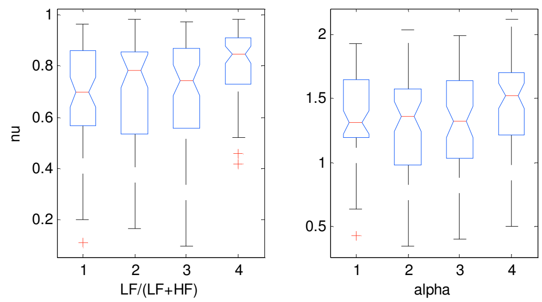

Figure 4. LF/(LF+HF) and α_1 evolution

4. Discussion and conclusions

Parasympathetic variability, depicted in the first factorial axis, decreases during PTCA and then tends to return to the normal conditions (post-PTCA). Axis 2 shows that sympathetic activity increases during and after PTCA. These results suggest a decreased parasympathetic response during balloon occlusion and an increase of sympathetic response during the recovery period. This study made possible to outline parasympathetic and sympathetic drives in a few variables. Another notable observation from this study is that LF/(LF+HF) and α_1 are highly correlated.

We have found significant differences between the LCX group and the other groups. The LCX group seems to have the highest sympathetic profile. It will be interesting to investigate if these differences are related to the location of the occluded coronary artery.

Significant events related to the autonomic control of heart rate occurred during and after coronary artery occlusions. A reduction of vagal activity and of ANS complexity was observed during PTCA, but a significant increment of the sympathetic component of the ANS and an increase in the complexity of its response were found during the recovery period after coronary occlusion. MFA provides a very powerful tool allowing the confrontation of whole information to assess autonomic nervous activity; further study could be focused on the analysis of ischemia associated parameters and their relationship with ANS associated parameters.

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