POINCARE' PLOT ANALYSIS OF HEART RATE VARIABILITY IN STROKE PATIENTS

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Abstract: To evaluate the relationship between lesion's severity and Poincarè plots (PPlots) features, 20 first-ever stroke subjects and 10 healthy subjects were studied. Patients were divided in two groups according to single or multiple medium cerebral artery lesion, All subjects underwent 24-hour Holter recording analysed by PPlots, spectral and time-domain techniques.

PPlots were quantified by the length (L), width (W) and area (A) of 2D plots and by the number of peaks (Np) and the length of the radii of inertia (Px,y,z) of the 3D plots. The power in VLF, LF and HF bands and the classical time-domain indices SDNN, PNN50, MSSD were also evaluated.

A direct relationship between increasing lesion's severity and progressive collapsing of both 2D and 3D PPlots was observed. L, A and Np, showed the most significant differences between groups, while lower significance was found for spectral and time-domain parameters. These results suggest that PPlots analysis contains relevant information related to different HRV dynamics in normal and stroke subjects with different lesion's severity.

Introduction

Cerebrovascular diseases represent one of the major cause of death and disability in western countries. An impaired cardiovascular autonomic regulation has been described in stroke patients with dysfunction that often complicate the clinical course of these pathology.

It has been hypothesized that these abnormalities are mediated by the central nervous system as a result of the cerebrovascular event, whereas the mechanism of this phenomenon is not fully understood [1,2].

The analysis of heart rate variability is a well recognized non-invasive tool to investigate the cardiovascular autonomic control but only limited data are available on the autonomic imbalance assessment of stroke patients by heart rate variability changes after a prior single stroke, using time- and frequency-domain linear methods [3,4].

Recently non-linear analysis of heart rate variability has been suggested to provide more valuable information for physiological interpretation of heart rate fluctuation and for the risk assessment [5].

Poincarè's plots (PPlots) analysis of beat-to-beat time series is one of these few methods that have been tested in clinical settings in the last years, allowing to detect patterns resulting from non-linear processes that may not be observable by time- and frequency-domain analysis [6,7].

It has been shown that Poincarè plots of heart rate variability allow quantitative display of parasympathetic nervous activity [8] and that quantitative descriptors of Poincarè plots are better predictors of mortality in cardiac patients than time-domain conventional indexes [9].

Several Poincarè plots analysis' methods have been proposed in literature, but it has clearly been shown that most of them bring back to existing linear measure of heart rate variability [10] and only nongeometric techniques, such as scanning parameters [11], allow to detect patterns resulting from non-linear processes that cannot be detectable by time- and frequency-domain analysis.

The aim of the present paper was to evaluate the relationship between the lesion's severity of stroke patients and Poincarè plots novel computer-generated quantitative indexes, comparing results with the traditional time- and frequency-domain linear parameters of heart rate variability.

Study Population

The study population consisted of 20 patients consecutively admitted to Neurology Rehabilitation Division of "Salvatore Maugeri" Foundation. All subjects enrolled were over 45 years old, with a positive past medical history for previous first-ever stroke (ischemic and/or hemorrhagic), presence of neuromotor monolateral deficit at physical examination and FIM score between 40 and 60.

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Patients with congestive heart failure (IV NYHA functional class), renal, hepatic or pulmonary failures, cerebral neoplasm, severe cranial trauma, psychosis, FIM score <40 or >60, atrial fibrillation were excluded.

The study population was divided in two groups of 10 patients according to a CT finding of medium cerebral artery single (SL, mean-age 65±15 yrs) or multiple (ML, mean-age 68±7 yrs) lesion. The control group (N) consisted of 10 healthy subjects (mean-age 42±6 yrs). Table 1 shows some variables considered in SL and ML stroke patients (SP).

Table 1: Some variables in the SL and ML groups.

	SL-SP	**ML-SP**	**p**
Age	65.05±15.23	68.38±7.55	ns
Height	163.52±6.18	165.13±7.79	ns
BMI	27.84±3.96	26.42±3.77	ns
SBP	138.82±14.95	136.15±21.03	ns
DBP	87.65±9.03	79.23±25.32	ns
Hb	13.12±1.35	13.49±1.87	ns
Cholesterol	220.15±48.19	178.57±30.68	<0.01
ADL	4.62±1.94	5.19±1.72	ns
IADL	7.24±2.43	6.75±1.91	ns
Diabetes (%)	2 (9.5)	1 (6.3)	ns
Hypertension (%)	9 (42.9)	6 (37.5)	ns
Ejection fraction	56.49±11.41	56.29±7.94	ns
NYHA class	1.90±0.72	2.19±0.66	ns

Values are mean ± SD. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; Hb, hemoglobin; ADL, activity daily living; IADL, instrumental activity daily living.

Holter Analysis

The study population underwent a 24-hour Holter ECG recording by a portable three-channel tape recorder, processed by a Marquette 8000 T system with a sampling frequency of 128 Hz.

All recordings were performed while the patients were allowed to standing or sitting next to their beds. Other activities were not allowed.

In order to be considered eligible for the study, each recording had to have at least 12 hours of analyzable RR intervals in sinus rhythm. Moreover, this period had to include at least half of the nighttime (from 00:00 AM trough to 5:00 AM) and half of the daytime (from 7:30 AM trough to 11:30 PM) [12].

Each beat was labeled as normal or aberrant according to recognition by the algorithm for tape analysis and after an investigator's verification.

All RR time series were analysed by PPlots, spectral- and time-domain techniques.

Poincarè Plots Analysis

The Poincarè plots technique is based on the analysis of the maps constructed by plotting each RR interval against the preceding one.

Usually bi-dimensional (2D) Poincarè plots are visually classified into three typical patterns [3]: a comet-shaped pattern (C), with an increasing heart rate variability at lower heart rates, a torpedo-shaped pattern (T), with a reduced heart rate dispersion on the whole distribution, and a fan-shaped pattern (F), with a great dispersion in a narrow range of frequencies. One major limitation of this visual classification is the subjective evaluation of the plots.

To overcome this problem, the automatic quantification of Poincarè plots has been recently proposed by our group. Moreover our maps plotted the RR couple repetition's number as the third dimension. of the plot (Fig. 1).

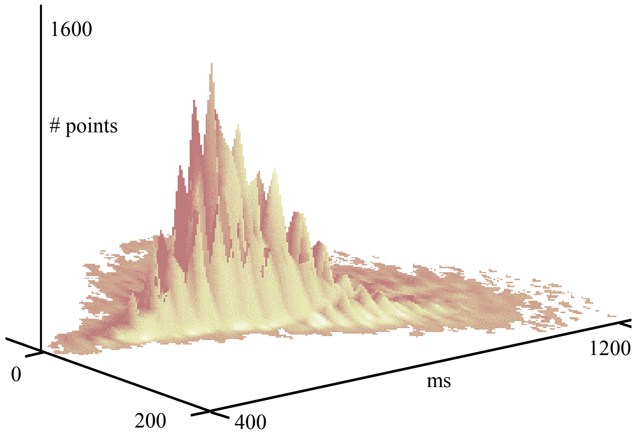

Figure 1: 3D Poincarè plots analysis

A dedicated software developed by the authors allowed to automatically calculate the main morphological characteristics of bi and three-dimensional (3D) maps. Technical details on the procedure have been described elsewhere and excellent reproducibility of obtained indexes has been previously demonstrated [11].

Only normal classified QRS complexes were considered in the analysis, excluding RR intervals preceding or following not-normal beats and plotting only time-closed RR couples.

The most meaningful parameters extracted from 2D PPlots are measures of the extension and dispersion of the ellipsoidal cloud of points around the bisecting line, namely the length (L), the area (A), the highest variability extension (HVE), that can be obtained scanning the plot with a vertical line and generating a curve which represent the measure of width of the scatter at different RR intervals, and percentage of length which corresponds the maximum plot wideness (P) (Figure 2).

The most interesting parameters extracted from 3D PPlots are measures related to the plot's height, taking into account the RR couples' repetition number, namely the peaks' number (Np), the mean peaks' distance from the bisecting line (Dp), and the length of the three radii of inertia (Px, Py, Pz) of the semi-ellipsoidal three-dimensional cloud of points (Figure 2).

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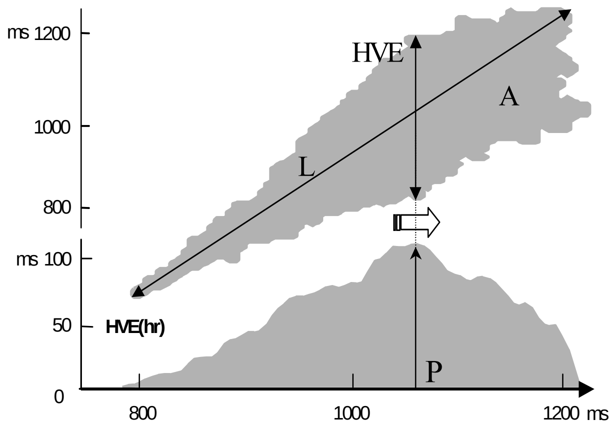

Figure 2: 2D Poincarè plots parameters

Linear Analysis

Spectral analysis was performed by an homemade software [13] on 5 minutes RR sequences extracted from 24-hours holter recordings automatically discarding sequences containing artifacts or large transients or containing over 4% of ectopies. The few ectopic beats present in accepted sequences were automatically corrected by an interpolating algorithm.

The original and the corrected 5 minutes sequences were plotted superimposed and the analyst could interactively decide whether to accept or to discard the resulting series.

Power spectral density was estimated by the Blackman-Tukey method in all accepted segments after linear trend removal. The total power and the power in the low frequency band (LF, 0.04-0.15 Hz) and high frequency band (HF, 0.15-0.45 Hz) were then computed by numerical integration of the spectral density function.

Most important time-domain parameters (SDNN, PNN50, MSSD) were also evaluated for all RR time series.

Statistical analysis was performed for all parameters by the Kruskal-Wallis test and the Dunn's post test for multiple comparisons.

Results

We observed a direct relationship between the increasing lesion's severity of stroke patients and a progressive collapsing of both 2D and 3D PPlots, indicating a progressive impairment of cardiac autonomic control.

L, A and Np parameters showed the most significant differences between the three study groups (Table 1), while lower significance levels were found for spectral parameters. There were no significant differences using time-domain indexes (only SDNN is shown in Table 2).

Table 2: Measurements in Normals and patients with Single and Multiple lesion of medium cerebral artery.

Index	**N**	**SL-SP**	**ML-SP**	**p**
L	803±108	518±103 °	436±87 **	<0.0001
A	16890±6357	16330±7071	9229±2840 **†	<0.01
Np	44±21	23±9	11±5 **†	<0.0001
VLF	684±202	1924±1221 °	1355±672	<0.005
LF	988±422	888±516	453±344 *	<0.05
SDNN	53±10	72±20	56±12	ns

Values are mean ± SD. ° SL *vs* N p<0.01; * ML *vs* N p<0.05; ** ML *vs* N p<0.01; †ML *vs* SL p<0.05.

Discussion

Our data clearly indicate that Poincarè plots indexes, in particular L, A and Np parameters are more sensitive than heart rate variability linear indexes in identification of autonomic nervous system impairment in patients after single stroke event.

Changes in Poincarè plots indexes seem to be significantly associated with different lesion's severity, suggesting a possible important role of the heart rate variability analysis also in the assessment of medium cerebral artery involvement after first-ever stroke.

On the other hand only few studies [1,2,14-17] found strong correlation between stroke and abnormal values of spectral content of HRV as well as a correlation with functional capabilities.

A further consideration may be done regarding the Poincarè plots technique that has been used. Many authors that used Poncarè's plots technique just paid their attention to the bi-dimensional indexes of the maps. Depending on the different estimation's methods, this class of parameters can be related to existing linear measures of HRV, hence the intrinsic ability of Poincarè' plot to identify non-linear beat-to-beat structure is not completely exploited by bi-dimensional maps alone.

An evidence supporting this consideration can be found in the statistical significance of the peaks' number (Np), one of the three-dimensional Poincarè plots indexes extracted, and in its discriminating power between the study groups. This suggests future improvements in the evaluation of other multi-dimensional Poincarè plot indexes.

In conclusion in the present study, heart rate variability was shown to be most markedly depressed in the patients with severe neurological deficits (multiple lesion *vs* single lesion and normal medium cerebral artery).

Poincarè plot indexes, particularly L, A and Np parameters, were the most sensitive markers of abnormal heart rate variability in our patients, compared to traditional spectral- and time-domain indexes.

Although further and wider investigations are needed for confirmation, these results clearly indicate that Poincarè plots analysis contains relevant information related to different heart rate variability dynamics of normal and stroke subjects with different lesion's severity.

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