Prognostic Value of Poincarè Plot Indexes in Chronic Heart Failure Patients

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Abstract

The identification of prognostic indexes in chronic heart failure patients represents a challenging task in the analysis of HRV. To this purpose we assessed the prognostic value of novel computer-generated quantitative descriptors of Poincarè plots (PPlots) of HRV in a case-control study over 13 CHF patients who experienced cardiac death and 13 matched CHF controls. All subjects had a Holter recording with computation of SDNN and PPlots analysis. While visual classification of PPlots and SDNN did not significantly differentiate controls from deceased patients, a highly significant association with outcome was found for quantitative PPlots indexes. This preliminary study shows that automatic quantification of PPlots allows a better discrimination between patients at risk of cardiac event and controls than visual classification of plot features and time-domain HRV.

1. Introduction

Despite recent advances in the management of chronic heart failure (CHF), the morbidity and mortality of these patients remains still high [1,2]

A clear flowchart for a risk stratification of these patients is still missing and a clear identification of most powerful prognostic factors would be needed to identify high-risk patients in whom a more aggressive therapy or heart transplantation may be suggested.

Beyond the importance of various clinical variables, such as functional class, left ventricular ejection fraction (LVEF), and peak oxygen consumption (peak VO2), the high prevalence of ventricular ectopy and ventricular tachycardia is a well known feature associated with heart failure, but it remains unclear whether ventricular arrhythmias identify patients at high risk of sudden death [3,4].

On the other hand, profound abnormalities in autonomic control, characterized by sympathetic overactivity and parasympathetic withdrawal, have been widely demonstrated in CHF patients [5,6].

The analysis of heart rate variability (HRV) is a well recognized non-invasive tool to investigate the autonomic cardiac control [7]. Recently, definitive evidence has been provided on the prognostic value of HRV for cardiac mortality independently of others risk stratifiers [8].

Although time- and frequency-domain linear parameters on 24-hour Holter recordings were shown to predict survivals in CHF independently of clinical and hemodynamic data [9], their value in clinical practice still remains to be completely determined [4].

It has been speculated that nonlinear analysis of HRV might provide more valuable information for the physiological interpretation of heart rate fluctuations and for the risk assessment in cardiac patients [7]. Among these techniques, Poincarè plots is one of the few methods that have been tested in the 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 [10]. It has been demonstrated that abnormal Poincarè bi-dimensional (2-D) plots, visually inspected and classified, are better predictors of mortality in heart failure patients than conventional indexes [11].

One major limitation of the Poincarè method is the subjective evaluation of the plots. To overcome this problem, the automatic quantification of morphological characteristics of 2-D and 3-D plots have been recently proposed by our group [12,13].

Aim of this study was to assess the prognostic value of this novel computer-generated quantitative descriptors of Poincarè plots of HRV in a case-control study on moderate-to-severe chronic heart failure patients who experienced cardiac death.

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2. Subjects and measurements

We considered for this study 13 male CHF patients, who experienced cardiac death during a follow-up of 26±19 months (median: 22).

Inclusion criteria were absence of pulmonary or neurological disease, absence of acute myocardial infarction or cardiac surgery within the previous 6 months, absence of any other disease limiting survival, stable therapy for at least 2 weeks and good quality 24-hour Holter recordings, with an ectopy rate < 5%.

An equal number of control subjects matched for age, sex, NYHA class and etiology was then selected (1:1 matching) from the same data set.

All subjects had a 24-hour Holter recording at baseline, together with standard functional evaluation including measurement of left ventricular ejection fraction (LVEF), peak VO2 and Sodium (Na). Holter recordings were manually edited by experienced analysts and corresponding annotated RR time series derived. HRV parameters were then computed, including the standard deviation of Normal-to-Normal intervals (SDNN) and Poincarè plot indexes (see below).

3. Poincarè plot analysis

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

According to other authors [10] the 2-D plots were classified by visual assessment into three typical patterns: a comet-shaped pattern (C), with an increasing HRV 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.

Poincarè plots were categorized independently by two analysts who had no knowledge of the subject's clinical data and were not involved in Holter analysis (100% agreement).

A dedicated software developed by the authors allowed to automatically calculate the main morphological parameters characterizing Poincarè maps.

Technical details on the procedure have been described elsewhere and excellent reproducibility of obtained indexes has been previously demonstrated [13,14]. 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 bi-dimensional plots are measures of the extension and dispersion of the ellipsoidal cloud of points around the bisecting line, namely the length (L), the area (A) and 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 scatterplot width at different RR intervals (Figure 1).

The most meaningful parameters extracted from three-dimensional plots are measures related to the plot's height, taking into account the RR couples' repetition number, such the length of the three radii of the semi-ellipse of inertia ρ_x, ρ_y, ρ_z (Figure 2).

4. Statistical analysis

Comparisons between cases and controls were performed by the Mann-Whitney and chi-square tests. The association between HRV parameters and cardiac death was assessed by univariate and multivariate logistic regression. Data are expressed as mean±SD. A p value < 0.05 was considered as statistically significant.

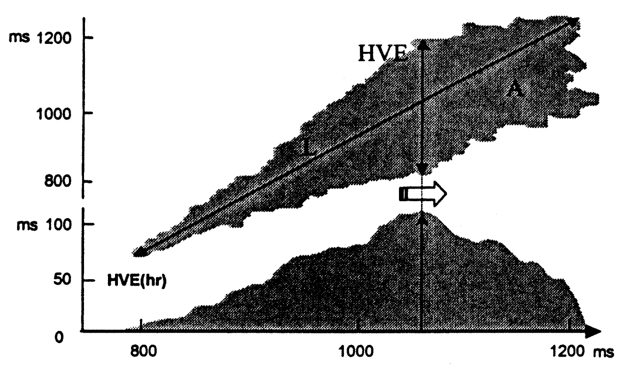

Figure 1. 2D Poincarè plots parameters

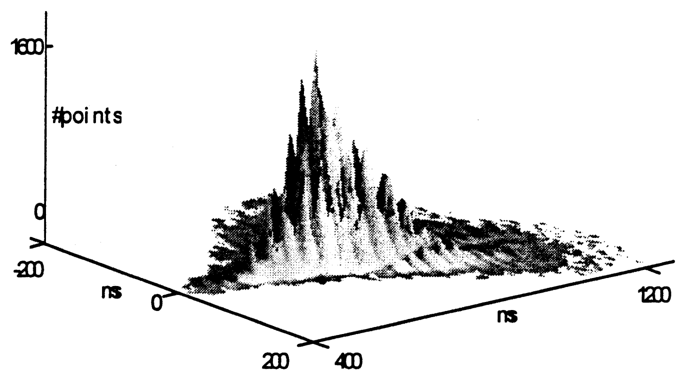

Figure 2. 3D Poincarè plots analysis

5. Results

Baseline clinical characteristics are shown in table 1. It is seen that the two groups of cases and controls were remarkably similar.

Table 1. Baseline clinical and functional characteristics.

	Cases	Controls	P value
N	13	13	
Age (years)	57±6	56±7	0.25
NYHA class II	9	9	
NYHA class III	4	4	
Ischemic	11	11	
Idiopathic	2	2	
LVEF (%)	23.4±3	23.4±3	0.8
Peak VO2 (ml/Kg/min)	14.2±3	15.1±3	0.47
Sodium (mEq/l)	138±2	139±3	0.54

Results for HRV measurements of SDNN and bi- and three-dimensional Poincarè plots parameters are reported in table 2. While SDNN, HVE and ρ_x parameters did not discriminate between the two populations, the L, A, ρ_z and ρ_y parameters showed significant differences between Cases an Controls subjects.

Table 2. HRV measurements.

	Cases	Controls	P value
SDNN (ms)	47.2±13	59.7±24	0.26
L (ms)	781±178	1006±272	0.03
HVE (ms)	272±107	331±123	0.24
A (ms^2)	9045±4006	14396±6412	0.012
ρ_x (ms)	51±11	47±13	0.35
ρ_y (ms)	95±11	120±27	0.008
ρ_z (ms)	81±18	112±36	0.015

The contingency table for visual classification of Poincarè plots is given in table 3. Although the classification patterns showed some differences between cases and controls, statistical significant was non reached (p=0.18).

Table 3. Visual classification of Poincarè plots.

Shape	Cases	Controls
Comet	4	8
Fan	3	3
Torpedo	6	2

Univariate results from logistic regression, given in table 4 showed a significant association of L, A, ρ_z and ρ_y parameters with outcome.

Table 4. Association between HRV measurements and outcome.

	Wald Chi χ^2	P value
SDNN (ms)	1.87	0.17
Visual classification	3.5	0.08
L (ms)	4.4	0.04
HVE (ms)	1.56	0.21
A (ms^2)	4.5	0.03
ρ_z (ms)	0.67	0.41
ρ_y (ms)	5.1	0.02
ρ_z (ms)	4.8	0.03

However, when these variables (L, A, ρ_y, ρ_z) were jointly analyzed through multivariate logistic regression, only ρ_y was found to be independently associated with the outcome (p=0.03).

6. Discussion

This preliminary study shows that automatic quantification of Poincarè plots allows a better discrimination between CHF patients at risk of cardiac event and controls than visual classification of plot features and time-domain HRV, as classically expressed by the standard deviation of normal-to-normal RR intervals.

The L, A, ρ_z and, particularly, the ρ_y parameters were significantly lower in patients who died of cardiac death; moreover, the same parameters were those significantly associated with the risk of death according to the logistic regression model. Hence, these findings indicate that these morphological features of Poincarè plots are those which more sensibly reflect the derangement in autonomic cardiac regulation that characterizes the subjects with worst prognosis in advanced heart failure.

Brower et al. [11] were the first investigators who provided evidence of a link between abnormal Poincaré plots, as assessed through visual classification, and poor prognosis in CHF patients. In our study, we observed some differences in the distribution of shapes (comet, fan and torpedo) between cases and controls. However, statistical tests failed to detect a significant relationship. Differences in the design of the two studies as well as in the clinical characteristics of the patients studied may account for such discrepancy.

Our exploratory investigation clearly suggest that objective evaluation of Poincarè plots through computer algorithms provides more accurate and clinically useful information than subjective classification of plot shapes.

As expected, Poincarè indexes were found to contain redundant information. Indeed, although 4 out of 6 parameters were significantly associated with outcome, only the ρ_y parameter maintained statistical significance when adjusted for the others. This suggests that a reduced Y radii of the semi-ellipse of inertia of the plot is the most powerful predictor of cardiac death and, in a sense, "contain" the prognostic information of the others.

These findings suggest that quantitative Poincarè plot indexes should be considered for inclusion in the candidate predictors' list of future large-scale prospective studies for risk stratification of CHF patients.

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