Visualisation of Heart Rate and Blood Pressure Dysregulation in Young Patients with Type 1 Diabetes Mellitus by Poincaré Plot

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Abstract

Time series analysis of cardiovascular signals is usually performed by linear methods. Inspired by an effort to apply nonlinear time series analysis into cardiovascular variability signals, the aim of this study was to compare heart rate and blood pressure variabilities (HRV and BPV) between young patients with type 1 diabetes mellitus (DM) and control subjects by Poincaré plot. We analysed supine rest HRV and BPV time series using Poincaré plot pattern analysis. The length and widths of Poincaré plot were evaluated by self-developed software. In patients with type 1 DM, we found significant reduction of all HRV Poincaré plot measures indicating heart rate dysregulation detected in visually understandable manner. However, no significant differences in BPV Poincaré plot measures were observed - we suggest that dysregulation of vessels` sympathetic control occurs later in the course of DM.

1. Introduction

The noninvasive assessment of spontaneous physiological parameters variations in time (physiological time series) can provide valuable information about control systems involved in their complex regulation. Time series analysis is able to provide data about normal dynamical system and its changes during pathological circumstances with clinically important applications (diagnosis, prognosis) [1, 2].

Time series analysis of physiological parameters is usually performed in time and frequency domains – by so called linear methods. The nonperiodic oscillations are ignored and usually regarded as a noise [1,3].

Cardiovascular control system components interact in a complex manner. These interactions are not linear – output is not proportional to input. The nonlinear systems are able to generate complex signals that cannot be distinguished from noise using linear tools. Therefore, there is an effort to apply nonlinear time series analysis methods into cardiovascular variability signals [1, 3].

Application of new mathematical tools based on nonlinear dynamics provides supplementary information about physiological control systems. However, computing of commonly used nonlinear parameters (e.g. correlation dimension) requires relatively long and stationary signals which are difficult to obtain from living humans. The graphical analysis by Poincaré plot is increasingly used because it can be performed from shorter data. Poincaré plot is on the boundary between linear methods and tools based on nonlinear dynamics – the principle of its construction is taken from the nonlinear dynamics theory, but parameters used for its quantification are essentially linear [4]. In addition, Poincaré plot enables to display information about beat-to-beat variability of heart rate in compact visual format which is easy to read [3].

Autonomic neuropathy is usually regarded as a late complications of diabetes mellitus (DM). However, autonomic nervous system dysregulation can be detected by modern sensitive methods even in early phases of DM [5]. Early diagnosis of autonomic neuropathy is important - the mortality of the patients with this complication is markedly higher [6].

The reduction of spontaneous heart rate variability (HRV) is an early sign of cardiac autonomic neuropathy [5]. HRV originates mostly from parasympathetic nervous traffic oscillations - HRV analysis can provide information mostly about vagal component of the autonomic nervous system [7]. On the other side, smooth muscles of the vessels are under dominant sympathetic control. Therefore, the analysis of blood pressure variability (BPV) can be more useful for detection of sympathetic dysfunction [8].

Relatively few studies were focused on cardiovascular dysregulation in young patients with type 1 DM. The aim of the study was to compare HRV and BPV Poincaré plot parameters between patients with DM and control subjects.

2. Methods

2.1. Subjects

We have investigated 17 young patients with type 1 DM (10 f, 7 m) aged 12.9 – 31.5 years. The mean duration of DM was 12.4 ± 1.2 years. The control group consisted of 17 healthy probands matched for sex and age.

2.2. Protocol

The length of R-R intervals was measured using telemetric system (VariaCardio TF4, Czech Republic) where ECG signal (sampling freqency 1000 Hz) from thoracic belt with electrodes was transferred into PC for further analysis. Systolic blood pressure (SBP) was monitored beat-to-beat using volume-clamp method by Finapres 2300 (Ohmeda, USA). The finger cuff was wrapped around middle phalanx of the third finger. Analog output of the Finapres was transferred into PC by analog-digital convertor PCL-711 (Advantech Co., Taiwan) with the sampling frequency of 500 Hz. The SBP values were obtained on-line using specially developed software and stored in PC for subsequent analysis.

The thoracic belt with ECG electrodes and finger cuff of Finapres device were applied after 10 min in sitting position. Then, the subject was in supine position on the bed during next 70 min of the continuous recording of the cardiovascular parameters.

2.3. Data analysis

HRV and BPV analysis was performed off-line in selected interval (interval started 30 min after reclining, the length of interval was 600 s) of the records using self-developed software.

We quantified several basic time domain HRV and BPV parameters: mean R-R interval duration (mean RR), standard deviation of the R-R intervals (SDRR), mean SBP and standard deviation of SBP values (SDSBP).

Poincaré plot is the semiquantitative tool for physiological parameters variability analysis which enable to assess their beat-to-beat changes. The HRV Poincaré plot is the scatterplot of current R-R interval length against the R-R interval length immediately preceding it and provides visually understandable information about both overall and beat-to-beat HRV. If the heart rate rhythm is regular then the points in plot are located close to the line of identity (4, 24). Analogously, BPV Poincaré plot is the scatterplot where x-coordinate of each point is the current SBP and y-coordinate is previous SBP value.

Poincaré plots of HRV and BPV were constructed from resampled R-R and SBP time series (1 Hz) and quantitatively analysed. Quantitative analysis of the Poincaré plot patterns (Fig. 1) was performed using self-developed software. The widths of Poincaré plot pattern at 10th, 25th, 50th, 75th and 90th percentiles of R-R intervals (SBP) distribution – W10, W25, W50, W75 and W90 were quantified.

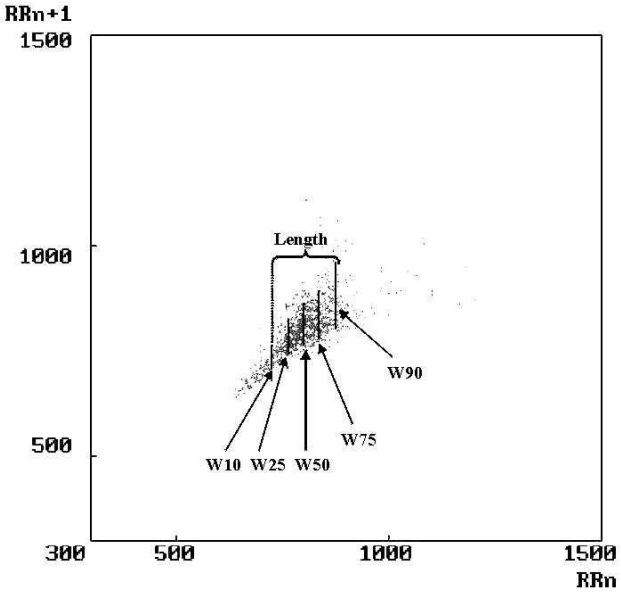

Fig.1: Poincaré plot (HRV) analysis with quantified measures

This approach enables to quantify beat-to-beat heart rate (and SBP) changes at given "basal" heart rate (SBP) level. The length of the Poincaré plot was defined as the difference between 10th and 90th percentiles of R-R intervals (SBP) distribution.

2.4. Statistics

Nonparametric tests were used due to non-gaussian distribution (ascertained by Lilliefors test) of HRV nad BPV parameters. Between-groups comparisons (DM vs control) were performed using Mann-Whitney U-test. All inferential statistics were considered significant at $P<0.05$ level and values are presented as mean ± SEM.

3. Results

Although mean RR tended to be lower in DM group, no statistically significant difference in mean R-R interval length between groups was found (control group: 903±30 ms; DM group: 825±29 ms; P=0.058). Significantly reduced overall HRV was reflected in SDRR (control group: 94±10 ms; DM group: 56±8 ms; P=0.017).

The example of typical HRV Poincaré plots for representative control subject and young diabetic patient are shown in Figure 2. Marked reduction in all measures of Poincaré plot pattern can be clearly

seen.

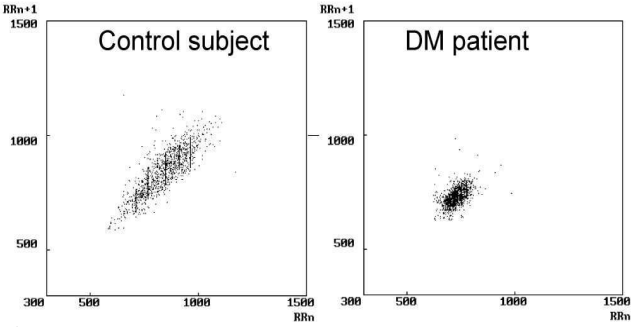

Fig.2: HRV Poincaré plots illustrate differences in beat-to-beat heart rate variability between a healthy control subject and a patient with DM. Marked reduction in all Poincaré plot indices was found in young DM patients.

Statistical analysis showed, that the length and all quantified widths (W10 to W90) of the Poincaré plot pattern constructed from the resampled R-R intervals were significantly lower in DM group compared to control group (Figure 3).

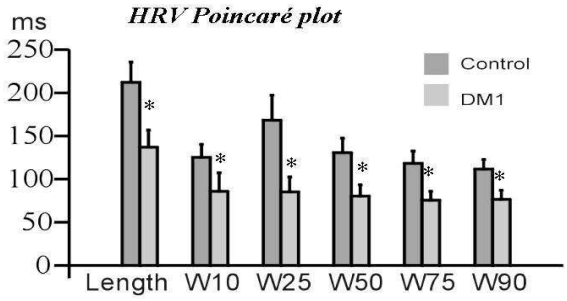

Fig.3: HRV Poincaré plot parameters in control subjects (dark gray) and patients with DM (light gray) presented as mean and SEM. Asterisks indicate significant between groups differences.

No significant difference in mean SBP (control: 117±3 mmHg; DM: 116±3 mmHg ; P=0.597) and SDSBP (control: 6.9±0.6 mmHg ; DM: 7.0±0.4 mmHg ; P=0.955) between groups was found. In addition, no significant differences between groups in BPV Poincaré plot parameters were found (Figure 4).

4. Discussion and conclusions

The characteristic findings in adult diabetic patients with autonomic neuropathy are resting tachycardia and reduced HRV, which is the earliest sign of cardiac autonomic dysfunction [5]. In our study we did not find significant difference in mean mean RR between diabetic patients and control group, but we found reduced overall HRV in young patients with DM. These findings are in agreement with other studies (e.g. [9]).

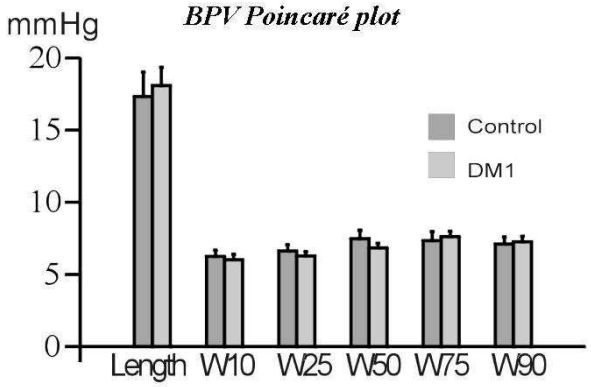

Fig.4: BPV Poincaré plot parameters in control subjects (dark gray) and patients with DM (light gray). Bars and error lines represent mean and SEM, respectively.

From the Poincaré plot parameters, young diabetic patients had all measures of the pattern reduced. The studies of Kamen et al. [10], Tulppo et al. [11] and others confirmed the reduction of Poincaré plot pattern measures in situations linked with parasympathetic inhibition. In addition, Poincaré plot can provide supplementary information about beat-to-beat variability at various heart rates that is unavailable by time and frequency domain analysis [3]. These findings indicate dysfunction of the parasympathetic component of autonomic nervous system in DM patients, because the short-term HRV is mostly mediated by vagal nerve discharge changes [7].

In contrast, short term blood pressure changes are mediated mostly by sympathetic nevous system and therefore the analysis of short term BPV has been taken as more sensitive for detection of sympathetic dysregulation than HRV analysis [8].

Several authors observed dysfunction of sympathetic control of the vessels in diabetic patients manifested as an reduction of spectral power in low frequency band in systolic blood pressure and skin blood flow signals [6]. Mésangeau et al. [12] found reduced standard deviation of blood pressure signal in animals with induced type 1 DM. In contrast, Chau et al. [9] did not observe changes in overall BPV in DM patients compared to control group. In our study no significant changes in overall systolic BPV were found.

We hypothesized that Poincaré plot analysis could be able to detect subtle abnormalities in beat-to-beat SBP control in young patients with DM. However, no significant changes in BPV quantified by Poincaré plot

pattern measures was observed in our group of patients compared to control group. We suggest that the significant sympathetic nervous system dysfunction was not present in our group of young diabetic patients.

In conclusion, Poincaré plot constructed from R-R intervals was able to reveal beat-to-beat HRV abnormalities. Poincaré plot can provide information potentially usable for diagnosis and prognosis in visually understandable manner. No significant difference between DM group and control group was observed in BPV quantified by Poincaré plot and standard deviation of SBP. We suggest that parasympathetic dysfunction in cardiac chronotropic regulation occurs earlier than dysregulation of sympathetic control of the vessels in young diabetics.

Acknowledgements

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