Heart rate turbulence and heart rate variability in patients with diabetes mellitus.

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ABSTRACT: Heart rate variability (HRV) and heart rate turbulence (HRT) illustrate regulation of the heart by autonomic nervous system. Diabetic autonomic neuropathy is a serious and common complication of diabetes. The aim of our study was to determine the association between HRT, HRV and diabetes control monitored by concentrations of HbA1c. In 56 patients with diabetes mellitus t. 2 24-hour Holter ECG monitoring was performed to evaluate time domain HRV parameters (SDNN, SDNNI, SDANN, rMSSD, pNN50) and HRT parameters (TO and TS). Regression analysis was performed to evaluate the association between tested parameters. We observed significant correlation between TO and SDNN, SDNNI and SDANN. TS correlated significantly with SDNN, SDNNI, SDANN, rMSSD, pNN50. We noted no correlation between HbA1c and HRV or HRT parameters.
We concluded that HRV time domain parameters correlate with HRT in patients with diabetes mellitus. Diabetes control estimated on basis of HbA1c value did not show correlation with HRV and HRT.

INTRODUCTION: Heart rate variability (HRV) and heart rate turbulence (HRT) depicts the functional status of the autonomic nervous system. Diabetic autonomic neuropathy is a serious and common complication of diabetes mellitus (DM)[1]. Dysfunction of the autonomic nervous system is associated with increased risk of mortality in patients with diabetes.[2]
In the present study we analyze correlations between HRV and HRT parameters and HbA1c in patients with diabetes mellitus.

MATERIAL AND METHODS:
The study group consisted of 56 patients with non-insulin depended DM. Clinical characteristics of the studied patients are shown in table 1.

Table1. Clinical characteristics of the studied patients

Parameters:	N(%) or mean ± SD
Number of patients	56
Gender (females/males)	36 (64%) M / 20 (36%) F
Age (years)	64,4 ± 7,6 years
Duration of diabetes	3 ± 1.5 years
Hemoglobin A1c concentrations	7.51% ± 2.84%
Insulin therapy	15 (27%)
Oral antidiabetic agents: sulphonylureas	35 (45%)
Oral antidiabetic agents: biguanides	5 (9%)

We excluded patients without sinus rhythm, after myocardial infarction and with left ventricular systolic dysfunction in echocardiography (EF<50%).

All patients underwent 24-hour Holter monitoring (12-channel recorders OXFORD SUPRIMA 12). Holter ECG was firstly analyzed automatically, followed by manual correction by the operator. HRV was analyzed in the time domain in accordance with standards[3] – all artifacts, arrhythmias, pauses and conduction disturbances were eliminated. We analyzed following HRV parameters:

- SDNN: Standard deviation of all NN (normal-normal) intervals
- SDNNI: Mean of the standard deviations of all NN intervals for all 5-minute segments of the entire recording
- SDANN: Standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording
- rMSSD: The square root of the mean of the sum of the squares of differences between adjacent NN intervals
- pNN50: NN50 count divided by the total number of all NN intervals

In patients with ventricular beats (PVC) we analyzed HRT parameters. HRT was quantified by two numerical parameters, namely the Turbulence Onset (TO) and the Turbulence Slope (TS).

TO is the percentage difference between the heart rate immediately following PVC and the heart rate immediately preceding PVC. It is calculated using the equation:

$$TO = ((RR1 + RR2) - (RR-2 + RR-1)) / (RR-2 + RR-1) * 100$$

with RR-2 and RR-1 being the first two normal intervals preceding the PVC and RR1 and RR2 the first two normal intervals following the PVC.[4]

TS is the steepest slope of a linear regression line through five consecutive measurement points in the averaged tachogram.[4]

We used filters which exclude RR intervals with the following characteristics from the HRT calculation:

- R-R < 300 ms
- R-R > 2000 ms
- Difference to the preceding sinus interval > 200 ms
- Difference to the reference interval (mean of the 5 last sinus intervals) > 20%

In addition, we limit the HRT calculations to PVCs with:

- a minimum prematurity of 20% and
- a post-extrasystole interval which was at least 20% longer than the normal interval.

We measured glycosylated hemoglobin (HbA1c) concentrations in all patients to evaluation of glycaemic control.

STATISTICAL ANALYSIS. The Statistica software was used. The results are presented as a mean ± standard deviation. Correlations were assessed using Spearman's rank correlation test. A p value <0.05 was considered statistically significant.

RESULTS. In study group HbA1c concentrations was from 5.9% to 10.2% (mean 7.51% ± 2.84%) In 11 (20%) patients the HRT parameters could not be computed (did not appear ventricular beats or ventricular beats did not meet criteria of HRT analysis).

HRV parameters calculated in subgroup in which it was not been possible to calculate HRT did not differ significantly from remaining studied group. HRV values and correlation coefficients between HRV and TO, TS, HbA1c are shown in table 2. Correlation coefficients between HRT parameters and HbA1c are shown in table 3.

Table 2. HRV values and correlation coefficients between HRV and TO, TS, HbA1c

HRV parameter	Value ± SD	Correlation coefficient with TO		Correlation coefficient with TS		Correlation coefficient with HbA1c	
		r	p	r	p	r	P
SDNN	130 ± 33	-0,33	0,005	0,52	<0,001	-0,12	NS
SDNNI	46 ± 16	-0,21	0,01	0,48	0,003	-0,14	NS
SDANN	122 ± 29	-0,26	0,003	0,42	<0,001	-0,12	NS
rMSSD	31 ± 13	-0,12	NS	0,36	0,005	-0,18	NS
pNN50	9 ± 8	-0,14	NS	0,32	0,005	-0,16	NS

Table 3. HRT values and correlation coefficients with HbA1c.

HRT parameter	Value	Correlation coefficient with HbA1c	
		r	p
TO	-1,1 ± 1,4	0,18	NS
TS	12,1 ± 9,5	-0,12	NS

We observed significant correlation between TO and SDNN, SDNNI and SDANN. TS correlated significantly with SDNN, SDNNI, SDANN,. rMSSD, pNN50.

We noted no correlation between HbA1c and HRV or HRT parameters.

DISCUSSION: HRT is the physiological, bi-phasic response of the sinus node to premature ventricular contractions. It consists of a short initial acceleration followed by a deceleration of the heart rate. The underlying mechanisms of HRT is an autonomous baro-reflex. It consists of a short initial acceleration followed by a deceleration of the heart rate causes a brief disturbance of the arterial blood pressure. If the autonomic control system is impaired, this reaction is either weakened or entirely missing.[5]

HRV describe variations of both instantaneous heart rate and RR intervals. Depressed HRV can be used as a predictor of risk after acute MI and as an early warning sign of diabetic neuropathy. In neuropathy associated with diabetes mellitus characterized by alteration of small nerve fibers, a reduction in time domain parameters of HRV seems not only to carry negative prognostic value but also to precede the clinical expression of autonomic neuropathy.[3,6] Correlations between HRT and HRV parameters was observed in large populations of patients after myocardial infarction (EMIAT and ATRAMI)[7,8]. Our study confirms significant correlation between HRT and time domain HRV in patients with diabetes mellitus.

Interesting is lack of correlations between time domain HRV parameters or HRT and concentrations of HbA1c. Previous studies have shown decreased heart rate variability in diabetic patients as a result of diabetic neuropathy, but frequency of occurrence of neuropathy have not correlate directly with HbA1c.[1]

CONCLUSIONS: We conclude that HRT parameters are under significant influence of autonomic nervous system and they correlates with time domain HRV parameters. Diabetes control judged by measurement of HbA1c concentration did not show correlation with HRV and HRT values.

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