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Heart rate variability in patients with systemic sclerosis

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Objectives. Heart rate variability depends on the state of the autonomic nervous system as well as on the state of heart muscle. It may be possible that some signs or symptoms of the heart involvement in systemic sclerosis patients result from the recently recognized autonomic nervous system manifestations.

Methods. Heart rate variability was determined by an integral computer-based standard system in 18 patients with systemic sclerosis (but only the results of 15 patients were statistically analysed) and 15 age- and sex-matched controls.

Results. A decrease in the mean RR interval and its standard deviation, as well as in the percentage of the difference between the consecutive RR intervals lasting longer than 50 ms was shown. The fractal dimension of Hausdorff was also decreased in the SSc patients. No changes of HRV parameters in patients with SSc were observed throughout the duration of their illness. However, a difference in the value of HRV, both in healthy and sick patients, was found.

Conclusions. There were no differences between the subgroups of patients with short-lasting (less than 8 years) and long-lasting (more than 10 years) symptoms of disease.

Statistically significant differences of HRV parameters between SSc patients and the control group were found.

On the basis of all the above clinical observations, we recommend further follow-up studies of this subject.

Key words: electrocardiographic recording, heart fibrosis, autonomic neuropathy

INTRODUCTION

Systemic sclerosis (SSc) is a general disorder of the connective tissue, involving a number of internal organs (1). Cardiac manifestations of SSc are common and they are associated with fibrosis of the myocardium and impaired coronary perfusion (2–4). It is possible that some of the signs or symptoms of heart involvement in SSc patients result from the recently recognized autonomous nervous system manifestations. Heart rate variability depends on the state of the autonomous nervous system, as well as on the state of the heart muscle (5, 6).

Klimiuk et al. (7), using the Valsalva maneuver, reported a decreased ratio of the longest RR interval to the shortest RR interval in SSc patients compared to healthy individuals. Morelli et al. (8) reported a decrease in the ratio of density of the low frequency power spectrum to the high frequency power spectrum in SSc patients. They used a standard 24-hour electrocardiographic monitoring system.

The aim of the present study was a comparison of heart rate variability in SSc patients and in healthy individuals.

MATERIALS AND METHODS

Investigations were carried out in 18 patients with definite SSc (16 women, 2 men) aged 42 to 75 years (mean, 54.2 ± 9.3 years). Patients with circulatory,

respiratory or renal failure were excluded from the study. Additionally, patients with other factors known to affect the sinus rhythm (age over 75, hypertension, diabetes mellitus, history of myocardial infarction) and receiving cardiac rhythm influencing medication were also excluded (9–13). Three patients, initially included, were excluded from the final analysis due to significant cardiac rhythm disturbances which made the recording of the sinus rhythm impossible. The SSc patients were divided into two subgroups.

Patients

None of the examined patients, before SSc was diagnosed, had HRV parameters assessed.

At the point of being included into the study group, patients with SSc varied in their duration of illness, which is from the initial diagnosis till the day of examination had lasted one to twenty years.

Eight patients with illness duration of 1 to 8 years were categorized into subgroup A. The further seven patients (10 to 20 years) comprised subgroup B. There was no age difference between the subgroups.

Control values were obtained from 15 healthy individuals (10 women and 5 men) aged 41 to 72 years (mean, 53.2 ± 9.4 years).

An informed consent was obtained from all the subjects prior to the study.

Standard ECG and echocardiographic examination was carried out in both groups, i. e. patients and controls did not confirm symptoms of overt heart disease.

Heart rate variability was measured with an integral computer-based standard system (MEDEA Gliwice, Poland). The testing frequency of 500 Hz and a twelve-beat distribution were applied according to the recommendation of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (14).

The recording lasted from 5 to 8 min, and at least 401 ventricular complexes were analyzed. Heart rate variability was measured on the basis of time domain and frequency domain analysis. The following indices were calculated:

- mean RR interval of all recorded sinus excitations (mRR);
- standard deviation of all normal RR intervals (SDNN);
- percentage of difference between adjacent normal RR intervals that are greater than 50 ms (pBB50);
- total number of all RR intervals divided by the height of the histogram of all RR intervals expressed as percentage (HRV index);
- power spectral density calculated by the ratio of low to high frequency power (LF/HF) expressed as percentage.

The following bands of low and high frequency applied were 0.04–0.15 Hz and 0.15–0.4 Hz, respectively (7, 17, 18). The fast Fourier transformation according to the methods of Blackman and Harris was used for frequency analysis. Hausdorff's dimension was calculated as a quantitative index of fractal analysis.

The statistical significance of the differences was determined by the Student's t test.

RESULTS AND DISCUSSION

Data on the heart rate variability evaluation in the SSc patients are summarized in Table.

A decrease in the mean RR interval, SDNN and pBB50 was observed in SSc patients. The fractal Hausdorff dimension was also decreased. An increase in the HRV index was found in the SSc patients. There was no difference in the measured indices between the groups with SSc symptoms lasting less than 8 years and more than 10 years.

The obtained results indicate significant abnormalities in the heart rate variability in SSc patients. Our findings are concomitant with the studies of Morelli et al. (8). They reported an increase in the LF/HF ratio in SSc patients, although they did not reveal alternations in other indices of time domain analysis. The differences between the results reported by Morelli et al. (8) and our data are probably caused by the different methods applied. They used the 24-hour electrocardiographic recording, while in the present study an integral computer-based system was used.

It is difficult to determine the detailed mechanism responsible for the observed alterations in heart rate variability in SSc patients. The described abnormalities are believed to result from primary autonomic dysfunction. Autonomic neuropathy is becoming increasingly recognized in patients with SSc (7, 16, 17). On the other hand, profound structural and functional changes in the hearts of SSc patients are widely reported, including rhythm disturbances which are believed to be early signs of cardiac involvement (2, 18). The lack of a relationship between the duration of the symptoms and heart rate variability is probably caused by variations in organ involvement and the course of the disease. In the flow of time SSc influences both the nervous system and the internal organs. Although the patient group with SSc was scarce, a trial to estimate HRV parameters according to the duration of illness was undertaken.

The parameter index HRV counted as the RR interval ratio of the most frequent occurrence compared to all analyzed RR intervals is by many scientists considered as the most applicable and functional parameter of time domain (19, 20) because of the way of achieving this parameter, which eliminates extreme values, as well as artefacts.

A significant statistical difference of the index HRV range between subgroup B (with long-time SSc duration) and control group ($p > 0.0321$) might suggest a correlation

Table. **Heart rate variability in patients with systemic sclerosis and healthy individuals (mean ± SEM)**

Index	Control group (n = 15)	Systemic sclerosis patients (n = 15)	SSc subgroup A (n = 8)	SSc subgroup B (n = 7)
mRR (ms)	911.57 ± 20.69	788.67 *a ± 23.79	788.98 *b ± 35.74	788.36 *b ± 33.58
SDNN (ms)	36.62 ± 2.29	25.74 *a ± 2.46	27.72 *c ± 3.61	23.68 *d ± 3.35
pBB50 (%)	3.29 ± 0.85	0.63 *a ± 0.31	0.44 *e ± 0.18	0.84 ± 0.66
HRV (%) index	13.53 ± 0.77	19.34 *a ± 1.61	19.03 ± 2.49	19.66 *e ± 2.16
LF/HF (%) ratio	46.16 ± 10.27	31.59 ± 7.98	35.15 ± 14.50	28.03 ± 3.69
Hausdorff's dimension	1.927 ± 1.437	1.878 *a ± 0.017	1.874 *c ± 2.724	1.880 *f ± 2.135

Statistical significance of the differences between SSc patients and controls.
*a: $p < 0.05$; *b: $p < 0.007$; *c: $p < 0.036$; *d: $p < 0.003$; *e: $p < 0.03$; *f: $p < 0.0436$. Statistical significance of the differences between subgroups A and B: all differences were not significant.

between a lower heart rate variability and sickness duration.

The parameter pBB50, assessing great changes of RR consecutive interval duration, correlates with the values of HF spectrum analysis, indicating parasympathicotonia (21).

A statistically significant difference in the values of pBB50 between subgroup A (with short-time SSc duration) and control group ($p > 0.03$) might indicate parasympathetic system impairment at the beginning of SSc. The capriciousness of the pBB50 parameter, already assessed by various scientists (21), is also emphasized in this paper and indicates the need for further studies of this phenomenon. Heart rate measurement variability seems to be a safe, relatively cheap, non-invasive method for evaluation of SSc cardiac manifestation. This method is recommended as a part of determination of internal organ involvement in SSc patients.

No changes of HRV parameters in SSc patients were observed throughout the duration of their illness. However, a difference in the value of HRV, both in healthy and sick patients, was found.

These observations might indicate that changes of HRV parameters appear at the initial stage of the disease.

CONCLUSIONS

There were no differences between the subgroups of patients with short- (less than 8 years) and long-lasting (more than 10 years) symptoms of the disease.

Statistically significant differences of HRV parameters between SSc patients and control group were found.

On the basis of all the above clinical observations, we recommend further follow-up studies of this subject.

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