Heart Rate Variability in Diabetic Patients During Orthostatic Load – A Spectral Analytic Approach

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Summary. Spectral analysis of heart rate variability (HRV) was used to assess the autonomic nervous control of cardiac function during orthostatic load in insulin-dependent diabetic patients and healthy subjects. The diabetic patients were divided into three groups: diabetics without neuropathy (group 1), diabetics with peripheral neuropathy (group 2), and diabetics with peripheral and autonomic neuropathy (group 3). Resting mid-frequency (MF, 0.05–0.15 Hz) and respiration-related (RF, power around respiration rate) HRV were significantly lower in group 2 and 3 diabetics than in controls, indicating a reduced parasympathetic nervous system influence on the heart. Standing MF and RF spectral power data were significantly lower in all diabetic groups than in controls, suggesting marked alterations in the autonomic cardiovascular control during a mild physical load not only in symptomatic diabetics but also in patients with no signs and symptoms of neuropathy. The difference between supine and standing MF power, an estimate of β-adrenergic influence on the heart, was significantly lower in all diabetic subject groups studied than in controls. This suggests a reduced sympathetic nervous system influence on the heart in diabetic patients. Our data suggest that computerized spectral analysis of HRV during orthostatic load seems to be a very sensitive method of evaluating the autonomic nervous systems influence on the heart in patients suffering from diabetes mellitus.

Key words: Spectral analysis – Heart rate variability – Diabetic subjects – Diabetic neuropathy – Orthostatic load

Cardiac autonomic neuropathy is a well-recognized complication of diabetes mellitus. Different methods of assessing cardiovascular autonomic nervous system function have been introduced, among them heart rate variation with deep rhythmic breathing and with the Valsalva maneuver, and heart rate and blood pressure responses upon sustained handgrip or standing [3]. However, no one of these tests can assess both divisions of the autonomic nervous system. Recent reports based on spectral analysis of heart rate variability (HRV) during orthostatic load describe the possibility to evaluate quantitative indices of the sympathetic and vagal influences on the heart [10, 11, 14]. The method of spectral analysis is utilized for the detection and quantitative description of periodicities in the heart rate fluctuations by deconvolution of the heart rate time series into sinusoidal functions of different frequencies [13]. Using these methods it is possible to partition the total HRV into its various constituents. Other authors [10, 11] as well as ourselves [14] have indicated that in human beings both divisions of the autonomic nervous system influence the HRV in a frequency-dependent way. These studies have shown that the respiration-related HRV represents an indirect estimate of vagal cardiac control, being abolished by atropine [11, 14]. The activation of the mid-frequency HRV during postural change from supine to upright seems to provide a useful marker of β-adrenergic cardiac control [10, 14]. Therefore, the present study was undertaken to provide quan-

Abbreviations: dB = decibel; HRV = heart rate variability; LF = low-frequency component; MF = mid-frequency component; RF = respiration related frequency component
 Subjects and Methods

**Subjects.** Thirty-six insulin-dependent diabetic patients participated in the study. They were divided into three groups based on neurologic history, neurologic examination, and nerve conduction studies. Group 1 consisted of 9 diabetic patients (6 males, 3 females) without clinical and electro-physiologic evidence (motor nerve conduction velocity in tibial nerve) of neuropathy. Their mean age was 26 (range 21–35) years; duration of diabetes ranged from 5 to 15 (median 10) years. Group 2 consisted of 16 diabetic patients (8 males, 8 females). These diabetics had symptomatic peripheral neuropathy and electrophysiological abnormalities. Their mean age was 34 (range 22–47) years; duration of diabetes ranged from 5 to 25 (median 13) years. Group 3 consisted of 11 diabetic patients (6 males, 5 females). These patients had evidence of peripheral neuropathy and complaints and signs of autonomic insufficiency (erectile impotence, sweat disturbances, nocturnal diarrhea, etc.). Their mean age was 38 (range 28–48) years; duration of diabetes ranged from 9 to 20 (median 15) years and was significantly longer as compared with duration of diabetes in group 1 (2P<0.01). The diabetic patients were taking no medications other than insulin.

The control group consisted of 24 healthy volunteers (20 males, 4 females) whose mean age was 34 (range 23–53) years. None of the healthy subjects were on any medication. All subjects had a normal systolic and diastolic blood pressure (<140/90 mmHg) at the moment of clinical examination. Studies were carried out between 9:30 and 12:00 h in a quiet room at a stable temperature (22°-24°C). Informed consent was obtained from all diabetic patients and healthy volunteers.

**Measurements.** The subject rested in a supine position, with recording transducers attached, for an adaptation period. At the end of this period, recording was started and after 10 min the subject stood up within 2–3 s, and remained motionless in the upright position for 12 min (with the first 2 min after standing up being excluded).

**Data Analysis.** During data collection the surface electrocardiogram (ECG) from standard lead and the respiratory signal from a nose-thermistor were measured continuously using a Biomonitor BST-102. The R-R intervals were determined in ms from the ECG and stored together with the low-pass filtered AD-converted respiratory signal (sampling rate 1 Hz) on a magnetic disc. The spectral analysis was performed off-line on 500-s stationary segments of variables recorded in both body positions. The heart beat series were passed through an ideal digital low-pass filter with a cut-off frequency of 0.5 Hz and sampled at 1 Hz [6]. The auto- and cross-correlation functions were computed and multiplied using the Papouls window and power spectra computed via Fourier Transform in a frequency band from 0.01–0.5 Hz with frequency intervals of 0.01 Hz. The coherence spectrum was bias corrected.

Spectral analysis focused on three periodic components of heart rate variability data [2, 7, 13]. One component is respiration related, determined as heart rate spectral power at respiratory peak frequency and -3 dB band width of respiration (RF). The second component is related to the so-called 10-s waves in the blood pressure (mid-frequency band, MF, 0.05–0.15 Hz). The third component typically occurs at frequencies lower than 0.05 Hz and should be attributed to thermoregulatory fluctuations in vasomotor tone and the renin-angiotensin control system (low-frequency band, LF, 0.01–0.05 Hz). The absolute and relative power of heart rate fluctuations at these frequency components were calculated. The total power (TP, variance of mean heart rate) and the peak frequency of the mid-frequency band, i.e., the frequency at the largest spectral density within this band, were determined. The differences between standing and supine values of mean heart rate (ΔHR), total power (ΔTP) and mid-frequency power (ΔMF) were calculated. The coherence spectrum is a measure of the amount of linear correlation between the variations of two signals, i.e., heart rate and respiration, at each frequency, calculated as mean squared coherence with its maximum around the breathing frequency.

**Statistical Analysis.** Results are presented as medians and 25 and 75 percentiles. Statistical comparisons were made with the Wilcoxon two-sample ranked-sum test and the two-tailed Mann-Whitney "U"-test. Because the HRV is dependent on age [5] and a significant difference in age was observed in diabetics of group 1 versus group 3 and controls (2P<0.01 and 2P<0.05, respectively) all values of variance and power spectral parameters were corrected with this exponential regression function.